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EMERGENCY AND PROPHYLACTIC CORTICOID THERAPY IN INDIVIDUALS PAST 50*†

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Clinical availability of corticotropin and cortisone, and the demonstration of their usefulness in rheumatoid arthritis (1) and other chronic destructive conditions, resulted in a great wave of enthusiasm among practicing physicians. When it became apparent that, in the course of suppressing certain diseases, undesirable effects of major magnitude could result from corticoid administration, the same voices which a little while before had been acclaiming the virtues of these hormones, were raised to denounce them as enemies of the race.

With the passage of time the dust has settled to a reasonable degree, and the legitimate place of these extremely valuable (as well as potentially dangerous) drugs begins to emerge.

There is general agreement that there is a place for their use in the management of a number of chronic diseases, particularly those such as pemphigus and lupus erythematosus, which are almost universally fatal without such therapy. There is also a majority opinion that they have a place in the management of patients with rheumatoid arthritis and related conditions. As yet, there is much disagreement as to when and how these agents should be used in these diseases.

In our own laboratory and clinic during the past several years, we have become increasingly impressed with the value of the corticoids in the management of certain acute emergency situations (notably unusually severe infections such as meningococcemia, meningitis, overwhelmingly severe peritonitis, and certain other infections), always in conjunction with intensive and well indicated antibiotic therapy.

During the past two years we have also begun to evaluate the place of cor-

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ticoids in patients past the age of 50 who are considered to be less than optimal operative risks.

EMERGENCY AND PROPHYLACTIC CORTICOID THERAPY—PRINCIPLES

The great bulk of our experience in this field has been in young children, and in adults past 60. Since this session is devoted to geriatrics rather than pediatrics, I shall limit my remarks to the latter group.

Before talking about clinical application, it may be well to consider some of the facts in regard to physiologic activity of compounds which have an overall cortisone-like effect. In this discussion, the term "corticoid" is applied to ACTH (corticotropin), cortisone, and hydrocortisone. ACTH stimulates the adrenal cortex to produce a variety of compounds having a net clinical effect which is similar to that of cortisone and hydrocortisone. Administration of sufficient amounts of any one, or a combination of these materials, will result in the following physiologic changes:

1. *Inhibition of the inflammatory reaction.* From a clinical standpoint, this can be good or bad, depending upon the initial clinical status of the individual and the method of administration of the hormones.

2. *Modification of membrane permeability.* Our knowledge of the regulation of cell membrane permeability is so limited, that we are unable to speak with any degree of precision. In a very nonspecific way, one might say that in patients who are in shock, or susceptible to shock, corticoids in proper amounts tend to keep within cells the things that belong there, and to keep outside of cells those things which should be outside, perhaps with particular reference to sodium and potassium. Thus they exert a net "anti-shock" effect.

3. *A net "nonspecific anti-toxic" effect.* This action of corticoids temporarily protects peripheral cells from a wide variety of circulating toxins of bacterial and other origins. It is most apparent when the corticoids are administered to patients who are extremely ill as the result of overwhelmingly severe infections. Such an effect was first described by Finland (2) in a patient with pneumococcus pneumonia. Administration of adequate amounts of corticoids to such individuals can result in complete or nearly complete disappearance of all clinical manifestations of disease, despite positive evidence of blood stream infection. It is obvious, therefore, that in the presence of known or suspected infections corticoids must be used with great care, inasmuch as they may render clinical detection of the disease virtually impossible.

4. *Increased blood volume.* Corticoids produce this effect by increasing the reabsorption of salt and water by the renal tubules. At the same time, they increase potassium loss by inhibiting renal tubular reabsorption of potassium, and probably also by actually mobilizing potassium from within cells.

5. *Increased protein catabolism.* Unless protein intake is high, corticoid administration results in a net depletion of the total protoplasmic mass.

From the standpoint of the clinical use of the corticoids in middle-aged and elderly individuals, if the physician considered any of the foregoing effects singly, he could be enthusiastic or apprehensive, depending upon the specific

item under scrutiny. If, for example, he concentrated upon the acceleration of protein catabolism, he might say that under no circumstances should one administer such agents to individuals who are in the age group in which the breakdown of tissue "normally" tends to exceed its rate of formation. If he looked superficially at the "nonspecific anti-toxic" effect, he might say that corticoids should by all means be administered to all middle-aged or elderly people who are exposed to minor or major infections or toxemias. In this connection, one is reminded of the fable of the three blind men, each of whom felt of a different part of the anatomy of a dog, and each of whom attempted to describe the entire animal on the basis of the single part which he happened to hold in his hand. The results were ludicrous, as one would predict.

On the basis of our own experience of the past four years, which is reasonably extensive, we believe that we may make some positive statements concerning the emergency use of corticoids in individuals past the age of 50, and some tentative statements concerning the prophylactic use of these drugs:

1. In elderly individuals with infections of more than usual severity (*i.e.*, infections which would not reasonably be expected to respond adequately to antibiotics alone) there will be a decrease in morbidity and mortality if corticoids are used in combination with antibiotics in a proper manner.

2. Corticoids should not be employed in the management of infections of average severity, *i.e.*, infections which will respond well to antibiotics alone.

3. Prompt and proper administration of corticoids, in conjunction with other indicated measures, in middle-aged and elderly individuals subjected to severe trauma, exerts a general anti-shock effect, and may lessen the likelihood of the renal shutdown which occurs so commonly under these circumstances.

I should perhaps present my own thoughts regarding the application of corticoids in one other emergency situation which is common in individuals past 50, namely, acute coronary occlusion. In animals in which coronary occlusion has been produced by surgical means, the survival rate is significantly increased when corticoids are administered (3). To the best of my knowledge, there are no data in the human which provide statistical proof of an increased survival rate when corticoids are administered to patients with spontaneously occurring coronary occlusion. We have as yet been unable to make up our minds as to whether corticoids are indicated or contraindicated under such circumstances. On the profit side of the ledger is the fact that they do tend to counteract shock, to decrease pain, and to produce a general sense of well being. On the debit side is the fact that they inhibit the inflammatory reaction. In patients with coronary occlusion, it is conceivable that such inhibition might result in rupture of the myocardium. Our present policy is to administer corticoids to such individuals only to combat severe shock, and to discontinue therapy (in a stepwise fashion) as soon as possible.

EMERGENCY CORTICOID THERAPY—PRACTICE

The term "emergency" is used here to designate the application of corticoids in individuals with overwhelming infections, toxemia, or shock from whatever cause. The basic rules which apply under such circumstances are:

1. Administer corticoids intensively, in association with adequate antibiotics.
2. Decrease the dosage in a stepwise fashion.
3. Always administer ACTH for one day longer than cortisone, to prevent any possible residual adrenal atrophy.
4. Administer corticoids for no longer than is absolutely necessary.
5. Continue antibiotics for at least three days after the discontinuance of all corticoids.

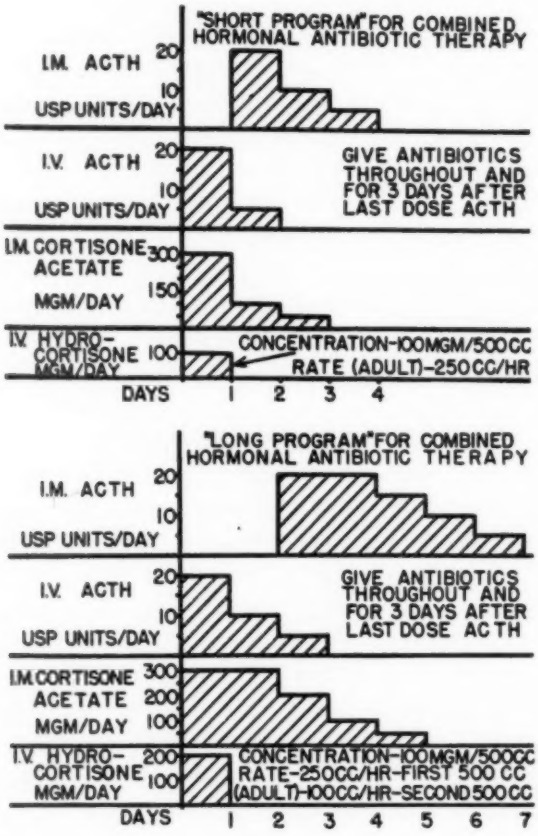

FIG. 1. "Standard" long-term and short-term emergency corticoid therapy. In addition to hydrocortisone infusion, hydrocortisone in propylene glycol (100 milligrams per 2 cc.) may be administered to patients who are in shock.

The application of these principles, as carried out in our own institution, is shown in Figure 1. Specific results have been discussed in a recent paper (4). It may be seen that we make use of a "short" and a "long" program. The decision as to which will be used depends upon the clinician's evaluation of the severity of the specific medical situation. In our hands, roughly 90 per cent of patients are put on the short program, and 10 per cent on the long program.

Adjuvant measures

It will be recalled that the corticoids cause: 1) retention of sodium, 2) loss of potassium, and 3) increased breakdown of protein. By and large, these effects

present greater problems in individuals who are on long-term corticoid therapy than in those who are treated for a period of a few days. Nevertheless, very serious situations may arise, particularly in debilitated elderly individuals, if these factors are not kept in mind. Most individuals receiving emergency therapy will be too ill to take food by mouth. It is, therefore, essential that they be maintained by means of parenteral or tube feeding—preferably the latter, if their physical condition permits. If the tube is used, the formula-feeding should be administered on an hourly basis throughout the twenty-four hours; for a person of average size it should contain 150 grams of protein and enough carbohydrate and fat to supply 3,000 to 4,000 calories. The sodium intake should not exceed 500 milligrams per day (unless the patient has been previously depleted of sodium as the result of vomiting or diarrhea); and the potassium intake should be in the range of 2 to 8 grams per day (unless the patient's renal function is impaired).

Daily determinations of serum sodium, potassium and chloride levels should be made if at all possible, and the dietary intake adjusted appropriately. Urinary output should be recorded constantly and fluid intake adjusted accordingly. The same statement applies to those individuals in whom gastric suction is used.

If intravenous feeding must be resorted to, caloric equilibrium is an impossibility, but proper attention must be paid to sodium, potassium, and chloride administration in line with the principles just noted.

One final precept—corticoids must never be administered to patients with surgical conditions, *e.g.*, generalized peritonitis, unless the decision is made to carry out definitive surgery the moment the patient's condition is at all suitable (usually within twenty-four hours after corticoid therapy is begun). To procrastinate in this regard is to bring about disaster. A patient with severe generalized peritonitis can appear well within twenty-four hours, only literally to disintegrate under one's eyes a few days later, *if corticoids are continued and surgery postponed.*

PROPHYLACTIC CORTICOID THERAPY—PRACTICE

By "prophylactic" corticoid therapy is meant the use of these hormones to prevent some possible dangerous or disastrous occurrence. Specifically, as previously noted, corticoids may be used in individuals who are to undergo surgical procedures and who are considered to be less than optimal subjects for such operations. However, one treads on much less firm ground in the field of prophylaxis than in the field of emergency application.

If we take a hypothetical patient, John Smith by name, aged 65, who is less than a "rugged individual" and who is to have a resection of a portion of his intestine, the physician will usually find it difficult to put into words precisely why he feels that John is less than an optimal subject for such an operation; nonetheless he is almost certain, on the basis of his clinical impressions, that such is the case. If he administers 50 milligrams of cortisone intramuscularly daily for two days prior to surgery and for two days thereafter, 25 milligrams daily together with 4 units of ACTH for two more days, and 4 units of ACTH

daily for a final two days, the patient may withstand the operation well and have an uneventful convalescence. There will obviously be a temptation to give some credit to the medication. It is equally obvious that it is impossible to say that the patient might not have done just as well without any hormonal medication. Nevertheless, it is our impression, based upon experience with approximately 40 John Smiths, that such a procedure is logical and desirable. We would have difficulty in proving this to our own, or anyone else's satisfaction. Perhaps the strongest argument in favor of such a regimen is the fact that if such an individual goes into shock following operation, the administration of corticoids can be very definitely helpful in overcoming the condition. Prophylaxis should be more logical than therapy.

If "prophylactic" corticoid therapy is to be used, it should be emphasized and re-emphasized that small dosage rather than large dosage is indicated (as opposed to the schedule in emergency procedures).

Other evidence which supports the rationale of prophylactic corticoid therapy concerns observations in patients who are subjected to adrenalectomy and hypophysectomy. Prior to the availability of cortisone, such procedures were impossible. The immediate cause of death in most instances was shock. Such patients, with adequate corticoid prophylaxis, usually have an uneventful convalescence.

CONTRAINDICATIONS

Contraindications to the administration of any agent in clinical medicine are relative rather than absolute. This is particularly true in the case of the corticoids. If this premise is accepted, the contraindications may be listed as follows:

1. Tuberculosis (danger of dissemination).
2. Diabetes (tendency to exacerbation).
3. Peptic ulcer (tendency to penetration and perforation).
4. History of psychotic episodes, or of major emotional instability.

In our own practice, if the urgency is sufficiently great, we proceed with corticoid therapy regardless of the presence of any of the foregoing conditions. Appropriate counter-measures are used, particularly in the case of peptic ulcer, for which intensive anti-acid medication is administered throughout the entire period of treatment.

SUMMARY

In middle-aged and elderly individuals with infections of more than average severity, the administration of corticoids in addition to properly indicated antibiotics appears to result in a decrease in morbidity and mortality. Corticoid therapy should not be used in the management of infections of average severity. When it is used in patients with severe infections, a precisely controlled program must be instituted.

There *may* be a place for prophylactic corticoid therapy in middle-aged and elderly individuals who are not optimal candidates for specific surgical procedures. The specific objective of such therapy is the prevention of operative or postoperative shock.

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THE INFLUENCE OF EMOTIONAL ATTITUDES ON THE AGING PROCESS*

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The tendency is normal for all of us to grow somewhat more rigid and hostile to change and new ideas as we grow older. In 1950, 42,000,000 Americans were over the age of 45 years, and 18,000,000 were over the age 65 years. If this tendency toward rigidity is allowed to proceed unchecked, its effects may be widespread. For example, the effect on the political status of our nation may be tremendous.

Older people are forced to retire and are often unable to obtain re-employment. There is a tendency to force them into a state of idleness, a feeling of uselessness, and a dependency on state and governmental agencies. There is reason to look on an approaching old age with fear of unhappiness, uselessness, and despair.

Richard L. Jenkins, in his new book *Breaking Patterns of Defeat*, says that our American culture gives to the ties of the new family (created by marriage) priority over the ties of the old (the parental family). As a nation we do not neglect our children, but we do tend to neglect our parents.

Although it is true that child health and child education are of tremendous importance, a parent should not be required to spend his later years feeling that he has outlived his usefulness. Our typical treatment of the aged makes their personalities more rusty than their joints.

THE STAGES OF LIFE

There are three stages of American life, each lasting from twenty to thirty years. The first of these includes childhood and adolescence and lasts until marriage. The second period lasts until children leave home—when the period of family life and child rearing is over. The third period is that readjustment lasting from twenty to thirty years when two people, who have often been too busy to know each other, are forced into a new relationship. Also, they are faced with the constant reminder that they are growing old. This strikes me forcibly as I grow older. People about 50 seem to want to tell me how old I am: "What does Old Dave say about that?"

Only recently has this last period been considered a part of American life. Now all of a sudden a new problem appears. We find that there is a possibility of just as much living, just as much happiness, and incidentally of just as much pain and unhappiness, in this third period of life as in the other two.

The inheritance, the biochemistry, the structural changes due to injury and disease, which the individual brings with him as he enters the third stage of

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life, have a great deal to do with the type of life he will lead. His emotional attitude also has much to do with his effectiveness.

There are those who say that we are as old as our arteries. There is definite evidence that cerebral blood flow and cerebral metabolism are related to personality functioning. As with many other things, we take it for granted that there has been a great deal of investigative work on cerebral blood flow and cerebral metabolism; but actual detailed, well-proven work is distinctly limited. Only a few investigators have been able to complete worthwhile studies.

Senile change is certainly related to cerebral thrombosis and cerebral softening, but are these structural changes in turn secondary to emotional factors, or do the behavior patterns of the later years depend upon vascular change? Certain persons have extensive evidence of vascular involvement. Necropsy of some of our most outstanding and capable men of great age has shown marked evidence of cerebral vascular arteriosclerosis.

EFFECT OF EMOTIONAL ATTITUDES ON AGING

I propose to present evidence of the effect of emotional attitudes on the aging process, by showing what can be learned 1) from a study of persons who have reached the later years of life without losing their normal faculties, 2) from a study of persons who have definite mental disorders, and 3) from opinions of those students of old-age reactions who have written on the effect of emotional attitudes on aging.

The history of mankind is replete with the story of men of advanced age who have functioned in excellent fashion. Moses was more than 80 years old when he led the Israelites out of Egypt. Clemenceau, the Tiger of France, was past 80 when he reached the peak of his fame during World War I. Winston Churchill is an outstanding oldster.

In every community several citizens stand out in this fashion. No one considers their age, because they function so adequately. Do these individuals have any characteristics that would give us the key to their success?

Dr. Martin Gumpert reports in *Pastoral Psychology* for September 1954, a study of individuals who have survived adequately to a great age. He states that their most outstanding qualities are the facts that they are interesting and interested in the affairs of life. He is certain that he would not have liked some of them in their younger years, nor would he have agreed with them. Now, however, they definitely have something of interest to offer.

In January 1954, a study of older people was reported in the *Journal of Diseases of the Nervous System*. Seventy persons were functioning well enough to live in a community; 52 lived in an institution. The average age of those in the community series was 70.9 years and those in the hospitalized group, 77.4 years. The investigators found a deep religious feeling in these people, but little interest in dogmas. Libido was maintained in 50 per cent. The ability to fall in love and to desire marriage appeared to be usual in people over the age of 70. Women apparently suffered more anxiety from lack of sexual outlet than did men.

Perhaps the best study on personality factors in aging is that just reported

in a book by Louise Bates Ames *et al.*, entitled *Rorschach Responses in Old Age*. The authors investigated 200 persons over 70, and under 100 years of age. All were reasonably healthy, active, and alert. There were 101 between the ages of 70 and 80 years, 86 aged 80 to 90 years, and 13 between 90 and 100 years old.

Forty-one, or approximately one fifth, gave normal responses. Twenty-seven of the 41 normal subjects were in their seventies, 11 in their eighties, and 3 in their nineties. Many were older in years than the members of the other two groups, which were classified as pre-senile and senile, respectively. In the normal group, the responses were characterized by their richness and variety. The same individual variations were found as in young adults. The pre-senile group showed rigidity, suspiciousness, and vagueness. Their emotional responses were shallow. There was some limited individual variation. In individuals in the senile group responses were very limited and restricted. They showed a tendency to repetition and inability to express emotion.

The study of these apparently healthy, alert adults indicates that normality in old age does not depend upon chronologic age, but upon the ability to maintain flexibility and appropriateness of emotional response. The study gives no clue to the secret of oldsters of age 90 who respond like young adults. The authors suggest the need for many chronologic studies in the same individual.

STUDIES ON ELDERLY INDIVIDUALS WITH MENTAL DISORDERS

Many studies have been made of the physiologic, sociologic, and psychologic nature of persons with senile psychoses. Kallman and Sander reported in 1949 a study of 1,602 twin index patients over 60 years of age. Basic physical and psychologic qualities, which were similar in the twins, tended to persist. A "variable capacity for survival" was found, which was thought to be inborn or characteristic of an individual.

Darkin and Kral reported the psychologic investigation of a case of senile dementia in *Geriatrics* for May–June 1951. They decided that the process of senile deterioration does not depend upon age, nor do all of the traits of a senile individual deteriorate. Some characteristics have a "capacity for survival." The findings of these two investigators indicate that much can be accomplished toward the rehabilitation of a senile individual if his surviving traits can be recognized and strengthened.

Felix Post indicates that an affective or content disorder, added to the picture in a person with senile change, is an aid in survival. It is well known that persons with paranoid and hallucinatory reactions tend to survive in mental hospitals, whereas the death rate of patients institutionalized because of senile dementia is eleven times greater than that of the general population.

These studies seem to indicate that a psychosis or neurosis developing in an oldster has survival value and perhaps checks the process of deterioration which leads to senile dementia and death.

Thus, the patient with a psychosis during old age is using his imagination and his emotional attitudes in his effort to survive. One of the youngest-appearing women of age 75 I have seen calls at my office every week to recount her fantastic experiences. They are a mixture of witchcraft and magic. We enjoy them together

and then she goes on to live her fascinating life in what would otherwise be a commonplace setting.

We have evidence, therefore, from the study of persons of great age who have maintained a normal dynamic equilibrium and from aged persons who have balanced the scale of life by abnormal means, that emotional factors do influence the aging process.

STUDY OF INVOLUTIONAL REACTIONS

In 1938, I began a study of involutional reactions. Initially, I worked with the families in which patients with such reactions lived. By studying family histories and investigating the type of family, I came to a fairly definite conclusion as to the type of person who is depressed in the involutional period. They are likely to be people from the middle-classes and to come from some of the best families. They have high standards of ethical behavior. Usually a family "theme" assumes considerable importance. Some of the families have education as their theme. In others, it is social standing. In Virginia, many families have been in the missionary field for many generations. In these families, with their need to help spread the gospel, there are undoubtedly many cases of depression.

Characteristic of the individuals themselves was the fact that they developed a certain technic for getting along in the world. Frequently they were of the restricted, rather compulsive type—the person who is chronically anxious, who starts as a worrier with a good deal of compunction and goes into the later period of life with a crucial shift into depression.

Other people also have very definite technics for getting along. Characteristically they confine themselves to one method. For instance, the hail-fellow-well-met is always a hail-fellow-well-met individual. The man who works very hard tries to solve everything by working very hard. Characteristic of the person who passes into a state of depression is the use of one technic—he puts all his eggs into one basket, so to speak, and has very little ability for variation. This may occur in the fifties and frequently it looks as if the male climacteric or the female menopause were the cause. I have tried endocrine therapy in some patients of this type, sometimes with startling effects; nevertheless in most instances it has not worked well. A great deal can be accomplished through the use of psychotherapy by persuading these people to become spontaneous, and enabling them to take on something new in life. Thus a process of extroversion is started again. Their interest turns from themselves to life outside.

I have seen many patients go through a period of depression, associated with weakness and loss of all sexual function, into a period where they again functioned adequately and continued to do so for many years. This was accomplished without glandular treatment. Electroshock therapy has been of value in many of these individuals.

NEEDS OF THE AGED

Walter B. Martin, President of the American Medical Association, talking on the human aspects of geriatrics at Old Point Comfort in September 1953, said that the needs of the aged are five in number. First is the maintenance of a sense

of continued usefulness. The second is an opportunity to work, partly for the purpose of maintaining income, but especially to sustain the feeling that the individual is useful and perhaps necessary. The third is a reasonable degree of physical health and comfort. Fourth is companionship, comfort, and affection from one's own family or old associates. The fifth need is financial security and independence of action. It is interesting that a physician should put social and emotional needs before those of physical health and financial support.

George Lawton in *Aging Successfully* speaks of a philosophy of maturity. He believes that preparation for old age should start at least by age 40. He emphasizes twenty-two ways to invite trouble after the age of 50. One should not eat too much or too little, not use sedatives for insomnia, not live in the past, nor be afraid of being old. The amount of "aliveness" one has, not the number of years one lives, determines age.

The elderly person should not concentrate on self-pity or security, but be venturesome within reason. He should say to the new idea, "I'll try it—not every new idea is bad, nor every change a revolution." Learning is a form of living, so something new should be learned each day.

Nathan W. Shock in *New Trends in Gerontology* feels that the greatest frustration in old age is not the loss of sexual power but the taboo put on the enjoying of romance by persons in their later years. Lawton has a Bill of Rights for elderly people and one of these is the Right to be Romantic.

There seems no doubt that some men maintain sexual potency to an advanced age, whereas others have the ability to indulge in sexual intercourse only on occasion. Complete impotence without organic defect in the male before the age of 60 years is probably of psychologic origin. Women also have sexual desire throughout life. As theirs is the passive role and as intercourse is always a possibility, they suffer more than men from the repression of the sexual desire. However, sexual intercourse never cured any serious psychologic disorder. After age 50, although it is a part of human relationship, actual sex plays less and less of a role. Sexual desire becomes more obsessional, as it is often part of the need of a man or woman who does not accept old age, to prove that he or she is still young.

Romance after the age of 60 brings joy to the heart, makes the fading eye shine once more, and gives the wrinkled cheek a rosy hue. But the romance is on a broader plane, involving a sharing of the whole personality. Marriage at the age of 70, if with a person of like age, is more apt to be successful than marriage in youth.

What we want through life is rather a peculiar thing. Unless there is complete involvement of the total being, sexual relations at no time in life bring satisfaction. We want to be regarded as persons of value and we want to be loved for ourselves as a whole. As we grow older and enter the old-age group, there is more of a possibility of that goal being realized than ever before.

Seward Hiltner, writing about the religious aspect of old age, points out that expansion is the characteristic of youth, whereas constriction comes with age. The aged must compensate by depth and intensity of reaction for the necessary

constriction of their lives. The ability to enjoy each moment and to appreciate living it as it is lived should be more characteristic of the aging man. Friends should be dearer and old objects more meaningful. He may not have a home, but life has to be lived and lived now, so he must live it intensely.

As friends drop off, it is important that new friends be made quickly to take the place of the old.

The ability to be one's self is the blessing of the aged. There is absence of the fear that others, seeing the capacity to love, will act vilely and thus break one's heart. One of the things we are afraid of through life is that, if we show ourselves as we really are, others will react in a way that hurts.

An ability to give something to others and interest in living undoubtedly are emotional attitudes which, if obtained, will go a long way toward establishing normal senescence and preventing senile change.

Let me grow lovely, growing old
So many fine things to do.
Laces and ivory and gold
And silks need not be new.
There is healing in old trees;
Old streets a glamour hold;
Why may not I, as well as these
Grow lovely, growing old?

CONCLUSIONS

It is fair at this point to draw certain conclusions from the foregoing discussion. In the first place, there is a capacity for survival in all human beings that is an inborn quality. This capacity for survival is characteristic of certain portions of the body as well as of certain traits of behavior. The traits capable of survival can be recognized and stressed, in order to check the aging process.

Secondly, the young years are the time for expansion, whereas the old years tend to produce constrictive behavior. The tendency to restrict can be met by emphasis on depth and intensity of living. Life after the age of 60 should be more meaningful. The small things are more appreciated and friends brought closer.

Thirdly, persons who retain their faculties to a great age are those who are interesting and have interests. They are people who still live useful lives, both from their point of view and from that of the community. Responsibilities aid the aged—even those who are senile.

Fourthly, active minds and emotions help to rehabilitate those portions of the total person that are capable of survival, even if the thoughts are distorted and the emotions react to stimuli that seem fantastic. That brings up the question of what should be done with older people who have, say, agitated depressions, or schizophrenic reactions? Individuals in older age groups have the same types of personality reactions as those in the younger groups. Not all of the mental diseases of old age are senile changes by any means. These people can be treated to advantage with insulin, cystine, or tyrosine. Nevertheless, these personality

reactions frequently have survival value that must be considered in determining the extent of treatment.

Fifthly, the taboo on romance for the aged should be lifted. Not that the nonsensical attempt by the oldster to relate to the youngster should be condoned, but it should be recognized that both men and women beyond the age of 60 or 70 years are capable of great and total love. In this love, the sexual component is of small importance.

Sixthly, there is a large portion of living in store for a number of people if they begin in the fourth decade to prepare for this period in which they can live the good life and live it more abundantly. Physical health and economic condition are important in the creation of this abundant life, but emotional attitude has a marked effect on the aging process.

There is a need to be spontaneous, to become interested in new things. Creative and spontaneous acts are of great therapeutic value. There is a real need to look forward, not backward.

In the days when the younger members of the family are taking over—which is a good thing—those in the older group should cease to be parents and be friends to their children. They should no longer be baby sitters or "suckers" on the younger generation. It is important that they should take their place, not in the past, but in an active generation—the generation of senior citizens.

PHYSIOLOGIC EFFECTS OF OBESITY UPON THE HEART

The Incidence of Obesity in Coronary Disease*

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It has been recognized for some time that overweight exerts a harmful effect upon cardiac function (1). It shortens life expectancy in normal persons and increases the mortality rate in those with heart disease by as much as 60 per cent (2–5). Conversely, when obese cardiac patients lose weight, their outlook is improved (6). The question arises whether obesity may actually cause coronary disease and hypertension. It is essential to collect data on these points, since heart disease and obesity are very common. Twenty-eight per cent of this country's population is at least 10 per cent overweight (7), and coronary disease is the major cause of death.

The physiologic effects of obesity on normal and diseased hearts will be reviewed and findings in a statistical study of obesity and coronary disease will be presented.

PHYSIOLOGIC EFFECTS OF OBESITY UPON THE HEART

Obese people often have symptoms suggestive of heart disease, but without any demonstrable cardiac abnormality. The commonest complaints are dyspnea, palpitation, fatigability and ankle edema (1). At first, the cause of these symptoms was assumed to be fatty infiltration of the heart. This suggestion was originally presented by Laennec (8), but has been discarded, as postmortem studies in obese persons show only an increased collection of epicardial fat, particularly over the right ventricle and in the interventricular groove (9). Occasionally, the fat may infiltrate into the muscle of the right ventricle. Some authors have assumed that these changes may cause atrophy of the right ventricle, congestive failure, or sudden death. Of this, there is no proof. Hirsch (10) found that in obesity the heart was relatively small for the body weight and reasoned that it was therefore relatively inefficient.

A more tenable explanation for the cardiovascular complaints which appear in noncomplicated obesity was advanced by Master and E. T. Oppenheimer (1) and, later, by Proger and Dennig (11). Master and Oppenheimer, using their original "two-step" exercise test (12), found the pulse rate and blood pressure increased and the work tolerance decreased in overweight people. Following reduction in weight, there was a drop in blood pressure and pulse rate, and the patients lost their symptoms. Their series included 53 patients who lost 25 to 30 pounds; the fall in systolic blood pressure on the average was 25 to 30 mm.; in diastolic, 15 to 20 mm.; and in pulse rate, 15 to 20 beats per minute. Proger and Dennig observed that in obesity the cardiac output and A-V oxygen dif-

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ference were normal after exercise, but that the vital capacity was diminished. The cardiac and respiratory rates, the level of blood lactic acid, the oxygen consumption and the oxygen debt were increased. The respirations were more shallow and rapid than normal.

Both groups of workers concluded that in obesity the heart was not inherently abnormal, but that there was a mechanical interference with cardiac function, resulting from the elevation of the diaphragm and upward displacement of the heart, which led to smaller and more rapid cardiac contractions. In the teleoroentgenograms the heart lay in a horizontal position and appeared enlarged, the apex being displaced outward to the left. This contour could be easily mistaken for cardiac enlargement. Also, the respiratory movements were limited and the lungs compressed, causing a reduction in vital capacity. Another possible factor embarrassing the heart was the extra load imposed by the fatty tissue, which required an increased capillary bed.

Obesity, per se, does not produce significant abnormalities in the electrocardiogram. Master and Oppenheimer pointed out the frequency of left axis deviation and inversion of P3 and T3 in obese persons, which they attributed to the transverse position of the heart (1). Other electrocardiographic changes have been reported (13, 14) in a small number of obese people, but it is possible that these were associated with some degree of cardiac enlargement.

As far back as 1900 Hirschfeld (15) had been led to conclude, on theoretical grounds, that undernutrition lightened the work of the heart—a view that was confirmed by later investigators. In 1919 Benedict and his co-workers (16) subjected people of normal weight to undernutrition and observed a drop in oxygen consumption, basal metabolic rate, pulse rate and blood pressure. Lusk (17) and DuBois (18) were fully aware of the beneficial effect of a low basal metabolism on the heart.

Subsequently Master, Stricker, Grishman and Dack (19) showed that in normal, obese patients the cardiac work was increased as a result of an increase in surface area and, therefore, in the total body metabolism and oxygen consumption. They started 5 overweight ambulatory patients on a 1,200-calorie diet. After an average weight loss of 12 per cent, they observed a drop of 13 per cent in oxygen consumption, a rise of 36 per cent in the A-V oxygen difference, a fall of 30 per cent in cardiac output, and of 35 per cent in cardiac work. The pulse rate and blood pressure also were reduced. The increased A-V oxygen difference indicated improved oxygen utilization.

The following case report from their article illustrates these findings: J. F., a woman 64 inches tall and weighing 179 pounds, lost 22 pounds in two months on a 1,200-calorie diet. The oxygen consumption fell 16 per cent and the A-V oxygen difference increased 13 per cent. The cardiac work fell from 4.3 to 2.9 kilogram-meters per minute. It was concluded that undernutrition is important in the treatment of cardiac patients, particularly those who are overweight, since loss of weight increases cardiac reserve and combats the tendency to heart failure and anginal pain.

Master, Jaffe and Dack (20, 21) observed beneficial results in patients with an anginal syndrome or acute coronary occlusion during administration of an

800-calorie diet. In coronary occlusion the mortality rate was significantly reduced as compared to the control group. The patients in the control group had received the cardiac diet generally given at that time, *i.e.*, a high-carbohydrate liquid diet, averaging over 2,000 calories.

In most of the patients the basal metabolism rate dropped to about −20 per cent two to four weeks after institution of the 800-calorie diet. The level of the basal metabolism could be varied by altering the caloric intake. The reduction in metabolism was associated with a fall in pulse rate, blood pressure and oxygen consumption. In a typical case the cardiac output was 2.76 liters per minute when the basal metabolic rate was −34 per cent, and it rose to 4.15 liters per minute when the metabolic rate was only −5 per cent. The findings are similar to those in hypothyroidism (22) but in these coronary patients the undernutrition did not produce clinical evidence of hypothyroidism or other untoward effects, even when the metabolism fell to −30 per cent or lower. The drop in metabolism appears to be a protective adaptation of the body to the low caloric intake. Proger and Magendantz (23) used a low-calorie diet successfully in treating congestive failure.

CORONARY DISEASE AND OBESITY

Opinions differ concerning the frequency of obesity in coronary disease. It has often been stated that coronary disease and occlusion occur more commonly in the obese (5, 9, 24–26); and these conditions were found to occur more frequently in overweight army officers (27, 28). In postmortem material, also, Wilens found coronary disease much more frequently in overweight persons and relatively rarely in the undernourished (29). On the other hand, careful studies in young men with coronary disease revealed no significant increase in the frequency of obesity (30, 31), and the results of one of these investigations suggested that coronary disease was more common in persons of mesomorphic habitus than in the obese.

In investigating the frequency of obesity in coronary disease, 1,000 consecutive patients seen in consultation were employed. The cases of coronary disease were classified as angina pectoris, acute coronary insufficiency, and acute coronary occlusion. In addition, the patients were grouped as underweight, average weight, overweight, and obese, according to the universally employed standard weight tables set up in 1912. The frequency of each weight group was then compared with that of similar weight classifications recently established in a large control series of cases (32) (Table 1).

Angina pectoris and acute coronary insufficiency

There were 100 males and 100 females with chronic anginal syndromes. Overweight was common among the males, the frequency of overweight and obesity being about twice that in the controls—39.0 *vs.* 20.1 per cent (Table 2).

Of 139 patients who had had at least one attack of acute coronary insufficiency, 113 were males. They also revealed a frequency of overweight and obesity twice as great as that in the control group—39.0 *vs.* 20.1 per cent (Table 3).

TABLE 1

*Classification By Weight Groups of Employed Persons, Based on a Sample From Unselected Records of About 74,000 Persons in 16 Industrial Plants and Army Air Fields (Civilian Personnel)**

Age and Weight Group		Males		Females	
		No.	Per cent of total	No.	Per cent of total
20–29 years	Total	1,316	100.0	1,426	100.0
Underweight—10% or more		296	22.5	406	28.5
Average weight		724	55.0	726	50.8
Overweight—10 to 24%		219	16.6	159	11.2
Overweight—25% or more		77	5.9	135	9.5
30–39 years	Total	1,175	100.0	1,262	100.0
Underweight—10% or more		320	27.2	337	26.7
Average weight		574	48.9	550	43.6
Overweight—10 to 24%		206	17.5	191	15.1
Overweight—25% or more		75	6.4	184	14.6
40–49 years	Total	1,034	100.0	1,141	100.0
Underweight—10% or more		340	32.9	324	28.4
Average weight		494	47.8	490	43.0
Overweight—10 to 24%		145	14.0	183	16.0
Overweight—25% or more		55	5.3	144	12.6
50–59 years	Total	1,036	100.0	1,099	100.0
Underweight—10% or more		366	35.3	326	29.7
Average weight		483	46.7	462	42.0
Overweight—10 to 24%		140	13.5	183	16.7
Overweight—25% or more		47	4.5	128	11.6

* The figures in this and in the following tables, are taken from Master, A. M., Jaffe, H. L. and Chesky, K.: Relationship of Obesity to Coronary Disease and Hypertension, *J.A.M.A.* **153:** 1499 (Dec. 26) 1953.

TABLE 2

Angina Pectoris in Relation to Standard Weight

Weight Group	Males, per cent of total		Females, per cent of total	
	Sample 100.0	Control 100.0	Sample 100.0	Control 100.0
Underweight	12.0	30.3	29.0	29.4
Average weight	49.0	48.6	52.0	43.9
Overweight	32.0	14.8	15.0	15.1
Obese	7.0	5.3	4.0	11.5
	39.0	20.1		

Total cases, male, 100; total cases, female, 100.

TABLE 3

Coronary Insufficiency in Relation to Standard Weight

Weight Group	Males, per cent of total		Females, per cent of total	
	Sample 100.0	Control 100.0	Sample 100.0	Control 100.0
Underweight	4.4	30.3	11.5	29.4
Average weight	56.6	48.6	61.8	43.9
Overweight	33.6	14.8	19.2	15.1
Obese	5.4	5.3	7.5	11.5
	39.0	20.1		

Total cases, male, 113; total cases, female, 26.

TABLE 4

Coronary Occlusion in Relation to Standard Weight

Weight Group	Male, per cent of total	
	Sample 100.0	Control 100.0
Underweight (10% or under)	8.0	30.3
Average weight	43.0	48.6
Overweight (10 to 24% or more)	33.0	14.8
Obese (25% or more)	16.0	5.3
	49.0	20.1

Total cases, male, 100.

There was no significant increase in overweight and obesity among the females.

Coronary occlusion

As in the foregoing groups, 100 male patients with previous coronary occlusion showed a frequency of overweight and obesity twice as great as in the controls —49.0 *vs.* 20.1 per cent (Table 4). It was necessary to know the weight before the coronary attack, because after the attack most of the patients had lost considerable weight on low-calorie diets.

COMMENT

Although these findings indicate that obesity is more common in persons with coronary disease than in other people, no conclusion may be drawn from them as to an etiologic relationship between the two conditions. It may be that a similar metabolic disturbance is present in both obesity and coronary disease. This is suggested by the observation that the S_f particles in the blood are increased in obesity or coronary disease (33). Further investigation is required to clarify the relationship.

SUMMARY

The relation of obesity to heart disease has been reviewed. New standards of weight and blood pressure for the population have become available. Obese people with heart disease have a much higher mortality rate than do those of average weight or less.

In uncomplicated obesity "cardiac" symptoms may appear, which probably are caused by mechanical and physiologic interference with the heart's function. The teleoroentgenogram of the heart may give an erroneous impression of enlargement. No significant changes appear in the electrocardiogram.

Obesity reduces work tolerance and cardiac reserve; it increases oxygen consumption, cardiac work, blood pressure and cardiac rate. Vital capacity after exercise is diminished.

Undernutrition lightens the work of the heart and has been of benefit to those with heart disease, because of a fall in oxygen consumption, cardiac output and cardiac work. The basal metabolism drops and the vital capacity increases. The introduction of a low-calorie diet in the treatment of coronary disease has lowered the mortality rate in coronary occlusion, and the tendency to anginal pain and congestive failure. Patients who make a complete functional recovery from coronary occlusion or coronary insufficiency present a low incidence of obesity.

The frequency of obesity in patients with coronary disease among 1,000 consecutive cardiac consultations was ascertained. There was a definite increase in the proportion of overweight in men with angina pectoris or acute coronary insufficiency. Obesity is a strain on the heart and is capable of producing or aggravating these types of coronary disease.

In acute coronary occlusion the incidence of overweight was also significantly increased over that in the general population.

In female patients, surprisingly, obesity was not more frequent than in the normal population. One possible reason for this finding may be that the females were few in number; also, perhaps they were seen after they had lost weight.

Although obesity is found more commonly in patients with coronary disease, no statement as to etiologic relationship is possible.

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STRENGTH OF OPINION AS AN INDICATION OF PHILOSOPHY OF LIFE; THE RELATIONSHIP BETWEEN STRENGTH OF OPINION AND ADJUSTMENT*

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The importance of a philosophy of life to individuals during their later years is frequently emphasized. This emphasis is chiefly based upon clinical evidence which, valid as it may be, is more useful in the development of hypotheses than in their establishment.

A more indisputable assessment of the relationship between philosophy of life and adjustment is dependent upon the recognition of manifest characteristics of life philosophy which may be measured and objectively evaluated in terms of the extent to which they are present among those who give evidence of being well adjusted or poorly adjusted. This was the purpose of the present investigation.

SAMPLE AND METHOD

The sample consisted of 76 middle-class and upper middle-class widows with a mean age of 68 years. These women resided in two college communities which were similar in population and in other respects. About half of the group was selected on the basis of suggestions by informants in the communities, and the other half was drawn consecutively from the registers of several Protestant churches. Informants were encouraged to list every person they knew who was a widow, unemployed or employed only part of the time, with at least a high school education. Of the 104 women with whom contact was established, 73 per cent agreed to cooperate.

The Burgess, Cavan, Havighurst Inventory (2, 3, 4) was applied to the entire group. Nine individuals with the highest adjustment score and 9 with the lowest score were selected for special study. This decision was made because the group proved to be homogeneous, with no scores which could be considered indicative of poor adjustment.[1] A correlational study might therefore have concealed a real relationship which would appear in only the extreme cases of a distribution with so little scatter.

Subjects were asked to evaluate proverbs according to the extent to which they agreed or disagreed with them. Ability to make definite decisions regarding feel-

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[1] The mean score of the "High" group was 73.2 and the mean score of the "Low" group was 48.8. Good adjustment is indicated by scores between 40 and 50, average adjustment by scores between 20 and 39, and poor adjustment by scores below 20. The groups described here represented excellent and good adjustment.

ings and beliefs pertaining to the proverbs was taken as the measure of a functioning philosophy of life. It was assumed that such a philosophy would serve as a guide or referent in forming opinions concerning the proverbs.

The investigator hypothesized that the "Highs" would make a clear declaration of their opinions, *i.e.*, they would check "Agree," "Strongly agree," "Disagree," or "Strongly disagree," rather than "Agree slightly more than disagree," or "Disagree slightly more than agree." The "Low" group, on the other hand, were expected to select neutral responses more frequently. The person who selects neutral responses seems to indicate that she is not sure of her beliefs regarding the matters under consideration.

This hypothesis was based, in part, upon interview observations of the manner in which a number of extremely well-adjusted women expressed their attitudes and beliefs. If this tendency toward positiveness were found among younger people, or among the maladjusted, one might consider it a kind of rigidity or restriction of personality generalization. Among women of this group it may represent a normal tendency for well-adjusted people to develop, as they mature, some philosophy which works for them and serves as a definite guide in making the many decisions and adjustments which life requires. This basic philosophy, a kind of hard core of belief, may then become an important aid to ego function, even though it may not in all instances seem to represent a way of thinking which would be conducive to optimum adjustment among people generally.

Proverbs were selected as a means of measuring opinions because they usually represent a definite way of looking at life which is succinctly and clearly expressed: "A proverb is a lot of life in a short sentence." Older people seem to like proverbs, possibly because they were often quoted to children of earlier generations, both at home and at school. This interest was found to be characteristic of women in the group. The proverbs differed from items in the Inventory used in determination of adjustment, in that a person could talk about her views in a general way without feeling that she was revealing information about personal matters. Considerable spontaneous discussion was elicited which supplied interesting insights into the thought processes of the subjects and seemed, in general, to be in congruity with the original hypothesis.

It was necessary to exercise considerable care in the selection of proverbs. The investigator did not want this technique to serve as a measure of high or low adjustment of the kind measured by the Inventory. Its purpose was to isolate a particular kind of response because of its assumed relationship to an important dimension of personality. If a majority of the proverbs selected expressed positive, optimistic attitudes, then well-adjusted women might tend to be sure of their agreement, whereas those who were less well adjusted might react with indecision. If a majority of the proverbs selected had certain subtleties of meaning which were negative, or pessimistic in implication, then women from the "Low" group might feel sure that they agreed with them because they served as an expression of their feelings, whereas the well-adjusted women might react with indecision.

Many proverbs were pre-tested in order to obtain four proverbs in each group which represented three points on a scale of general attitude for each area of life

being investigated.[2] The first proverb was intended to represent favorable, optimistic, "well adjusted" attitudes toward life; the next two to represent either favorable or unfavorable attitudes, depending upon the interpretation of the subject; and the last one to portray unfavorable attitudes. Each of the following eight groups was therefore set up in a uniform manner. However, when communicated to the subjects, a random order was used in each group in order to avoid always starting with a positive proverb.

A person is only as old as he feels.
Sickness teaches the value of health.
No one can have a peaceful life who thinks too much about lengthening it.
Without health life may not be lived to the fullest.

* *

Old friends are the best friends.
Prosperity makes many friends but in bad times friendships are proven.
Be friends with the friendly and visit those that visit you.
Love your friends but look out for yourself as well.

* *

Of the things that stay, let work be one of them.
Age should think while youth should do.
Work today and tomorrow's uncertainties will not stand in your way.
The time comes when no man is able to go on working.

* *

The best things in life are free.
To have money is a joy: not to have it an inconvenience.
Money is a good servant but a bad master.
People often miss a lot for the lack of a little money.

* *

More things are accomplished by prayer than this world dreams of.
Unselfishness is as real a religion as any.
A religious life is sometimes a joy and sometimes a struggle.
Religion depends upon wishful thinking.

* *

Nothing is so precious as time for the person who has good use for it.
Be a life long or short, its usefulness depends upon what it is lived for.
Only in useful tasks can one find satisfaction.
The day comes when a person looks up and there is no one for her to help.

* *

No wise man ever wished to be younger.
Life contains sorrows aplenty; after the sorrows come joy.
Nature gives us all a chance for happiness but few of us know how to use it.
Nothing brings more pain than too much pleasure.

* *

In the family, love and affection can last as long as time.
So many of the strengths and weaknesses of America are due to the kinds of families we have.
Relatives are God-given: we can choose our friends.
Age and youth together will strain a family's ties.

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[2] Proverbs representing health, friends, economic security, work, religion, usefulness, happiness, and family relationships were used. Seventeen graduate students in fields related to human behavior were used in preliminary selection of proverbs, which were then given to a group of seven psychologists who were asked to take the role of the subjects in their final evaluation. Unclear proverbs, trite proverbs, and those which could not be classified according to the various categories were eliminated. Positive and negative proverbs were also pretested and equated in terms of the amount of feeling which they could be expected to arouse, so that biases would not result as a consequence of pairing many "weak" positive proverbs with "strong" negative proverbs and vice versa.

Each subject was interviewed privately in her own home under very favorable conditions. In introducing the proverbs the interviewer simply said that the responses would give information regarding the way people think about things and that there were no right or wrong answers, since each person is entitled to her own opinions and opinions naturally differ. Each subject was given eight cards with four proverbs from each area of adjustment on a card, and was asked to mark down her own responses. "Favorable," "unfavorable" and "either way" proverbs appeared in random order on the cards.

RESULTS

Total responses of the "High" and "Low" groups to the proverbs are summarized below:

	High	*Low*
Strongly agree	100	73
Agree	77	107
Agree slightly more than disagree	27	55
Disagree slightly more than agree	18	11
Disagree	43	31
Strongly disagree	20	9
Not responding	3	2

The expected difference between the two groups on the "Agree" and "Disagree" options did not appear. The general trend of the responses was, however, in accordance with the hypothesis. The difference between the "Highs" and "Lows" with respect to the tendency of the "Lows" to choose the neutral items ("Agree slightly more than disagree," or "Disagree slightly more than agree") is significant: "High" total, 45; "Low" total, 66; ($X^2 = 3.96$ $p = .05$ with one degree of freedom). The tendency for the "Highs" to select the extreme options ("Strongly agree" or "Strongly disagree") is readily apparent: "High," 120; "Low," 82; ($X^2 = 7.14$ $p = .01$ with one degree of freedom).

DISCUSSION

An explanation for these findings other than the one which led to the development of the hypothesis should be considered. In some ways the making of decisions may have been easier for the "Highs," since their superior adjustment would be likely to induce them to express socially acceptable attitudes when agreeing with the proverbs indicative of favorable adjustment, disagreeing with "unfavorable" proverbs, and interpreting the "either way" proverbs favorably and agreeing with them. In support of this explanation, it was found that the "Highs" disagreed with "unfavorable" proverbs more frequently than did the "Lows." Nevertheless there is considerable evidence that the decision-making ability of the "Highs" was dependent upon factors other than the opportunities afforded them for expressing socially acceptable responses. They offered little more agreement with "favorable" proverbs than the "Lows" and presented as much disagreement with these proverbs as the "Lows." The "Highs" also expressed greater disagreement with the "either way" maxims than did women of the "Low" group. Since these proverbs may be interpreted in a manner indica-

tive of both favorable and unfavorable adjustment, this suggests that the ability of the "High" group to take a stand and disagree is not dependent upon the unfavorable orientation of the material. This disagreement with "either way" proverbs may also reflect the aversion to ambiguity which seemed to be characteristic of the "High" group. It is possible that both a more definite formation of opinion among the "Highs" and a kind of avoidance mechanism among the "Lows" account for the tendency for the "Lows" to choose neutral responses.

SUMMARY AND CONCLUSIONS

In order to provide an opportunity for a type of decision-making thought to be indicative of the presence of a functioning philosophy of life, 18 widows (9 women of excellent adjustment and 9 women of good adjustment) were given a list of thirty-two proverbs and were asked to evaluate each statement according to the extent of their agreement or disagreement. It was hypothesized that members of the "High" group would make a more definite declaration of their opinions than would women of the "Low" group. Underlying this hypothesis was the assumption that well-adjusted older persons can no longer afford to be tentative about their beliefs in many areas of life. They must develop some philosophy which works for them and serves as a definite guide in determining attitudes and behavior.

The tendency for the "Highs" to select extreme options and the tendency of the "Lows" to select neutral responses were both found to be statistically significant. The possibility that a kind of avoidance mechanism among the "Lows" may contribute to their preference for neutral items was considered. Evidence is cited which suggests that the "Highs" were able to make decisions on proverbs, irrespective of their content.

A relationship between strength of opinion and adjustment has been established under the conditions of this experiment. Further investigation of this variable, with similar and dissimilar methods and groups, should prove to be of considerable interest to those seeking understanding concerning the psychodynamics of successful adjustment during the later years.

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THE FLUID, ELECTROLYTE AND NUTRITIONAL MANAGEMENT OF THE ELDERLY SURGICAL PATIENT

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The correction of fluid and electrolyte deficits and maintenance of the surgical patient solely with parenteral alimentation can be simplified by several bedside tests which are easily carried out. These tests have been used by the Surgical Service at Highland Alameda County Hospital during the past two years. This discussion is directed primarily toward the elderly surgical patient, and is concerned with two objectives: 1) the correction of deficits in the surgical patient with acute and chronic fluid and electrolyte losses, and 2) the maintenance of balance postoperatively while the patient is receiving parenteral fluids.

FLUID AND ELECTROLYTE BALANCE

There are certain physiologic principles involved. 1. Dehydration implies not only the loss of water, but of salts such as sodium, potassium and chloride. 2. The starving individual who cannot sweat, secrete urine or lose fluids through respiration and defecation will lose about half a pound per twenty-four hours from tissue breakdown. 3. All loss in excess of this rate in the starving individual represents loss of water and electrolytes through the respiratory tract, genito-urinary tract, gastrointestinal tract, and skin. 4. Fractionation of fluids and electrolytes is quickly and efficiently accomplished by the normally functioning kidney.

Body weight. Most individuals know their normal weights within a few pounds. The normal weight of the patient and duration of his illness are the first means of obtaining an estimate of hydration. Calculations of replacement are based on the body weight, urinary output, gastro-intestinal losses, and the urinary chloride. For example, if a patient has been unable to take anything orally for six days and has lost 14 pounds in weight, it may be calculated that a total of 3 pounds, or half a pound per day, has been lost from tissue breakdown. The remaining 11-pound loss is from water and electrolyte deficiencies; thus 11 pounds of water and electrolytes must be given to correct the dehydration. Each liter of fluid administered intravenously weighs 2.2 pounds; therefore, it will take 5 liters of fluid to correct or replace the deficit.

Renal function. After calculation of the fluid deficit, the renal competence is estimated. If the bladder urine has a specific gravity of 1.016 or better on admission, there is good kidney function. An important ancillary bedside test is the determination of urinary phenolsulfonphthalein (PSP) excretion. If a dark pink or purple color is obtained upon alkalinizing a few drops of urine from fifteen to twenty minutes after the administration of PSP intravenously[1],

[1] 1 cc. of PSP given intravenously.

good kidney function and adequate renal blood flow are demonstrated. Urinary chloride excretion should also be determined[2]. Renal competence is further demonstrated if the urinary chloride level is low (10 mEq./L.), indicating the kidney's attempt to conserve salt. These three bedside tests can be performed quickly and easily, and provide an index of renal function in the dehydrated patient who is not in shock.

The blood. It is important to remember that chemical analysis of the blood does not provide a reliable means of evaluating the status of hydration and electrolyte depletion. Frequently, normal blood electrolyte values will be obtained when the patient is moderately dehydrated. If electrolyte values are abnormal, one can be sure either that dehydration is severe, that replacement has been markedly in error, or that the kidney function is impaired.

Intravenous fluids. Unknown factors in dehydration are the quantitative loss of fluid, its ionic content, and the rate at which the specific ionic losses have occurred; also unknown is the rate of restitution of intracellular normality when fluids and ions are supplied. The kidney filters water and salts inversely to the body's needs; given the necessary fluids and salts, it can selectively retain those needed to restore homeostasis. Parenteral fluid should be administered in such a way that further cellular dehydration does not occur before physiologic processes can establish a more normal internal environment, *e.g.*, if one is dealing with a dehydrated patient whose cells and extracellular spaces are small because of fluid and electrolyte loss, and whose circulating blood volume is low, a hypertonic solution given intravenously will compound an already precarious situation. Physiologic saline (containing 150 mEq. of sodium per liter) given to a severely depleted patient will cause further intracellular dehydration; in such a situation it acts as a hypertonic (electrolyte-wise) solution. To avoid this intracellular dehydration, 5 per cent glucose is given in saline solution containing only 75 mEq. of sodium per liter, in order to supply water and salt in a hypotonic state at the beginning of the correction.

Concomitantly with the onset of adequate urine production (20 cc./hour), *potassium* is added. The intravenous solution (5 per cent glucose in saline containing 75 mEq. of sodium per liter, with 25 mEq. of potassium, 10 mEq. of calcium and 10 mEq. of magnesium) is given at the rate of 1,000 cc. every two hours by constant drip. The individual who is deficient in water and sodium is generally deficient in potassium. If sodium and water are given without potassium, there is further depletion of the intracellular potassium because of its replacement by sodium. Administration of these various elements offers the kidney the building blocks with which to re-establish homeostasis of the internal environment. The electrocardiogram has not been as helpful as we first thought in recognizing potassium deficit. However, it is of distinct value in following the patient who is receiving potassium for replacement therapy, as T-wave changes and QRS changes manifest themselves when the higher levels of potassium are reached with increase in the intracellular potassium.

[2] Scribner, B. H.: Bedside determination of chloride, *Proc. Staff Meet., Mayo Clin.* **25**: 209–218 (Apr. 26) 1950.

Rehydration. Once rehydration has begun, how can its progress be assessed? The kidney can excrete chloride in minute quantities when the body is deficient in salt. As hydration progresses and electrolytes are replaced, the rate of chloride excretion also increases. One of our patients, who was deficient in salt, excreted as little as 3 mEq. of chloride per liter of urine. In any patient whose fluid and electrolyte losses have been replaced on a calculated basis, and in whom urinary chlorides assay 75 mEq. per liter, salt replacement has actually been accomplished. A special problem occurs in the patient with intestinal obstruction, whose weight is normal but who has from 4 to 5 liters of fluid trapped in loops of bowel. This trapped fluid is, for physiologic purposes, lost to the internal environment. In this instance the urinary chloride determination is helpful, because the fluid in the bowel is not only water but also electrolytes, the intracellular and extracellular deficits of which are reflected in the urinary chloride level. If the body weight has been restored to normal by administration of a calculated amount of fluid, but the urinary chloride concentration is only 10 to 12 mEq. per liter, the patient is still in need of saline. Administration of sodium chloride is continued until the urinary chloride level approaches or equals that (75 mEq. per liter) which is being given intravenously.

Postoperative period. This type of replacement therapy with "half-normal" saline (75 mEq. per liter), glucose, potassium and vitamins is continued, in spite of the known retention of sodium in the adrenocorticoid phase of stress response. It has been our observation that salt deficits are increased when sodium is withheld immediately postoperatively in patients *in whom dehydration and salt replacement were not achieved preoperatively* because of the urgency of surgical intervention.

The maintenance of fluid and electrolyte balance in the postoperative patient *who is already in balance at the time of operation* is relatively simple, if the source and volume of the losses are determined and the losses are replaced quantitatively in addition to the basic requirements. The elderly patient can ill afford to be "maintained" haphazardly or "routinely." There is no such thing as a routine schedule for the administration of intravenous fluids postoperatively. In recognition of the well-documented evidence for sodium retention in the immediate postoperative period, no sodium is given. The intravenous infusion consists of 2,000 cc. of 5 per cent glucose in water, with 500 mg. of ascorbic acid per liter and 3 cc. of a soluble vitamin B preparation per liter, during the first 24-hour period. This allows for 800 cc. of fluid loss in sweat and respiration and 1,200 cc. in the urine. After the first twenty-four hours there is a change to 1,000 cc. of 5 per cent glucose in "half-normal" saline and 1,000 cc. of 5 per cent glucose in water, with the same added vitamins. This allows for loss of 1 gram of sodium chloride through sweat and 3.5 grams in the urine. The loss from nasogastric suction is replaced quantitatively with 0.6 per cent saline (about 100 mEq. of chloride per liter)—the average chloride concentration in the stomach and small bowel. Potassium is replaced on the basis of 10–15 mEq. per liter of gastric juice or small-bowel fluid aspirated. If there is any excess sodium in this replacement, it is excreted by the kidney. Undiluted biliary losses

are replaced quantitatively, using a proportion of two-thirds 5 per cent glucose in saline and one-third ⅙ M lactate. Pancreatic loss is replaced, using a proportion of one-half 5 per cent glucose in saline and one-half ⅙ M lactate. In the last two replacements, 10 mEq. of potassium per liter is added to the solutions.

It is imperative that the patient be weighed accurately daily at the same time, to check the calculated replacement and to obtain warning of salt and fluid retention or unrecognized excessive loss through sweating.

Cardiac insufficiency. The elderly patient who is undergoing elective surgery may present some problems because of myocardial insufficiency and its attendant edema. Moreover, kidney function may not be as good as that of the younger patient or there may be a latent prostatic obstruction. Evaluation of these is important, in the event of possible future difficulties. Thorough investigation of renal function may be made preoperatively. If cardiac insufficiency as manifested by edema, ascites, and basilar pulmonary congestion is attacked energetically with mercurials, there is danger of hyponatremia. It is better to permit some peripheral edema rather than de-salt such patients too vigorously. They are the ones who require more meticulous observations of losses and accurate replacement. We undertake parenteral replacement for the cardiac patient by the same method as discussed previously. In addition, chloride determinations are made on the fluids lost from the gastro-intestinal and biliary tracts, so that such losses may be replaced more accurately.

Nutrition and metabolism. Further studies which should be made preoperatively in order to assess the nutritional and metabolic balances in the elderly patient are determinations of the blood levels of protein, creatinine, and prothrombin. These assays are useful in indicating the need for preoperative nutritional build-up as well as evaluating liver function and patency of the urinary tract —factors which are so important in the convalescent period. In the patient with a chronic debilitating disease, blood and plasma volume studies are carried out, using radioactive serum albumin.

Plasma and erythrocyte deficits are corrected with transfusions, not oftener than every other day. During this preparatory period, vitamins are given in excess of the daily normal requirements, with a nutritious diet (3,000–3,500 calories) containing approximately 1 gram of protein per pound of body weight. Tube feedings are used to achieve these levels, if the patient does not take the food orally. When sterilization of the bowel is necessary, broad-spectrum antibiotics are used, along with synthetic vitamin K in daily 10-mg. doses; these are continued postoperatively until the patient is eating well. Operation is undertaken when the patient's status is felt to be optimal, with a normal serum protein level, a prothrombin concentration of at least 70 per cent, and a normal hematocrit and blood volume.

This discussion is too short to take up the entire field of replacement of losses occurring through small-bowel fistulae and debilitating diarrhea, but the approach to the problem is similar.

SUMMARY

Methods for bedside evaluation and for treatment of the elderly surgical patient are outlined, whereby the replacement of fluid and electrolyte losses may be successfully achieved. The nutritional and hepatic aspects are definitely helpful in appraising and preparing the elderly patient for a major surgical procedure.

Acknowledgment

I wish to acknowledge the time, effort, and teaching of Dr. R. P. Lyon in working out this method of fluid and electrolyte management for surgical patients.

E. G. Thomas, M.D.

PULMONARY EMPHYSEMA: PHYSIOLOGIC FACTORS IN DIAGNOSIS AND ADVANCES IN THERAPY

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Pulmonary emphysema, as the term is generally used clinically, refers to an overinflation or distention of the lungs (localized or diffuse) by a relative increase in the amount of air which cannot be blown out with a forced expiration. In order to determine the total lung capacity (TLC), this residual air capacity must be measured and added to the vital capacity.

DEFINITIONS AND METHODS

Vital capacity

A satisfactory procedure for measuring vital capacity is from spirogram tracings made with an apparatus such as the Collins 13.5-liter respirometer (1). This method provides not only a dynamic recording of the total vital capacity but a volume measurement with respect to time (three seconds), and permits study of the characteristic features of the breathing curve (Fig. 1).

Vital capacity is commonly measured by having the individual take a deep breath and then blow out the air as far as possible. It may also be determined by having the subject first blow the air out of the lungs as far as possible and then take in a maximum deep breath. There is no evidence that the latter procedure is not as valid as the former, for clinical study. In the normal individual there is no significant difference between the results of the two methods, but in patients with pulmonary emphysema a more accurate value is frequently obtained by the second method. In either procedure, the measurement obtained is the volume difference between maximal inflation and maximal deflation of the lungs. The level of the diaphragm may shift with position and activity. For this reason, the determination of vital capacity in two separate steps (as the sum of inspiratory reserve and expiratory reserve) is subject to error. If the vital capacity is significantly greater when the patient is lying down than when he is standing up, a severe degree of pulmonary insufficiency is indicated.

Residual air capacity

Residual air capacity can be accurately measured by means of the oxygen open-circuit method (2, 3). The patient breathes oxygen for seven minutes, and all the expired air is collected in the large gasometer during the breathing period. Small samples of the air in the gasometer are analyzed for nitrogen, and from

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ERRATUM

In the article entitled "Pulmónary Emphysema: Physiologic Factors in Diagnosis and Advances in Therapy" by Hurley L. Motley and Reginald H. Smart, published in *J. Am. Geriat. Soc.* **3:** 316–329 (May) 1955, the words "of compressed air" should be omitted from lines 4 and 5 on page 324, and from the first line of the second paragraph of the Summary on page 328.

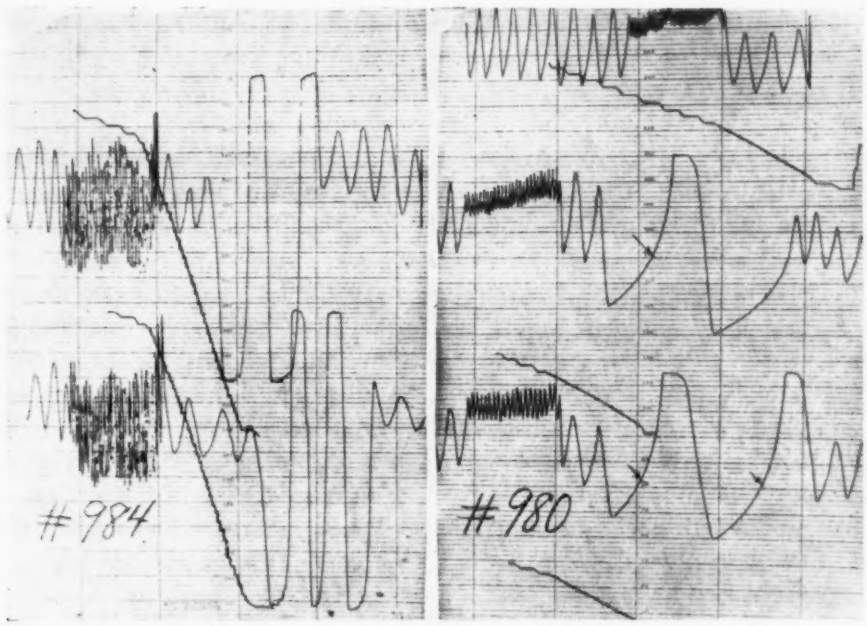

FIG. 1. Spirogram tracings of total vital capacity, the three-second timed vital capacity and the maximal breathing capacity, illustrating the characteristic features in a normal tracing (#984) and in a patient with severe emphysema (#980). Residual represents 61.6 per cent of total lung capacity. The time interval between the vertical lines is twelve seconds. In the case of severe emphysema (#980), the total vital capacity was 2,650 ml. (64.6 per cent of normal), the timed vital capacity for three seconds was 1,620 ml. (39.5 per cent of normal), and the maximal breathing capacity was 39.0 liters per minute (34.0 per cent of normal). The arrows drawn on the tracing #980 indicate the volume of air blown out during the first three seconds from the exact beginning of expiration. The slow exhalation curve obtained after taking a deep breath indicates a significant degree of pulmonary emphysema. The elevated level of the rapid breathing on the tracing during the twelve-second run for the maximal breathing capacity measurement is characteristic of pulmonary emphysema.

this percentage value the total volume of nitrogen washed out during the seven-minute period of breathing is computed. The volume of air which must have been in the lungs in order to contain the volume of nitrogen washed out can then be calculated, after making suitable corrections for the nitrogen diffusing from the blood during the period of oxygen breathing. In this laboratory, the residual air is routinely measured twice on each subject, and checks within 100 ml. are required; otherwise the procedure is repeated.

Total lung capacity

The residual air capacity plus the vital capacity equals the observed total lung capacity (TLC) for the individual case. In pulmonary emphysema, the TLC values may be at the normal predicted level, or they may be increased or decreased. Wide individual variations in TLC occur in patients with pulmonary emphysema; in some cases it may be increased as much as 40 per cent above,

and in other cases decreased more than 50 per cent below the normal predicted level.

Alveolar nitrogen

The percentage of alveolar nitrogen present after breathing oxygen for seven minutes is determined routinely as part of the residual air measurement. The alveolar nitrogen value provides an index of the uniformity of air distribution in the lung. In this laboratory, using the oxygen open-circuit method and a specially designed set of breathing valves with the alveolar nitrogen sampling orifice located just above the mouth piece, the normal value for alveolar nitrogen concentration is 1.5 per cent or less after breathing oxygen for seven minutes (3). An alveolar nitrogen concentration of 5 per cent or more indicates a marked lack of uniformity of air distribution in the lung. Even in the most severe cases of pulmonary emphysema the alveolar nitrogen concentration rarely exceeds 10 per cent. In some cases of pulmonary emphysema the percentage of alveolar nitrogen may be within the normal range, especially in individuals with a marked reduction in total lung capacity and in the presence of hyperventilation.

CLINICAL OBSERVATIONS IN EMPHYSEMA

The residual air normally occupies about 25 per cent of total lung capacity, being slightly less in the younger age group (20 per cent for adults under 35 years of age) and slightly more for individuals over 60 years of age (30 per cent). Data obtained in this laboratory from studies on 100 patients aged 15 to 70 years with normal spirogram tracings (including the total vital capacity, the timed vital capacity for three seconds, the maximal breathing capacity, and the shape of the exhalation curve) indicate that the increase in the residual air capacity with age is of small magnitude and normally does not exceed 35 per cent of total lung capacity (4). It is realized that many individuals having volumes of residual air which represent more than 35 per cent of total lung capacity are still working and may report no pulmonary complaints; but this does not mean that their lung volumes are normal, any more than a blood pressure of 200/140 is considered normal even though the patient has no complaints and may work for many years. There is a large breathing reserve in the normal lung, as attested by the fact that many individuals with one good lung get along remarkably well following a pneumonectomy. In general, when respiratory complaints are present in pulmonary emphysema the pathologic changes involved are very extensive.

Physiologic classification. Pulmonary emphysema may be classified on a quantitative basis by expressing the residual air volume as a percentage of total lung capacity. If the residual air occupies less than 35 and more than 25 per cent of total lung capacity, there is a slight, but insignificant degree of pulmonary emphysema; if the residual air occupies from 35 to 45 per cent, there is a moderate, but significant degree; if from 45 to 55 per cent, there is a severe degree; and above 55 per cent, a very severe degree of pulmonary emphysema. This classification has been found satisfactory, regardless of the etiologic factors in-

volved (3). In some cases the degree of pulmonary emphysema present as determined by the physiologic method is very poorly correlated with that demonstrated in x-ray films, or even by physical examination. Accurate residual air measurements remove the uncertainty from the evaluation of the amount of emphysema present and provide information which is valuable in clinical management of the individual case.

Maximal breathing capacity. (*The spirogram*). The spirogram tracings are better correlated with the quantitative measurements of pulmonary emphysema than are the results of any of the other readily available clinical tests. In men, if the maximal breathing capacity is over 120 liters per minute no significant degree of pulmonary emphysema is present (residual air less than 35 per cent of total lung capacity), but if the maximal breathing capacity is less than 40 liters per minute this measurement is correlated with a significant degree of pulmonary emphysema (5). On the other hand, a maximal breathing capacity between 40 and 120 liters is indeterminate with respect to the presence or absence of a significant degree of pulmonary emphysema. If the exhalation curve on the spirogram tracings is markedly prolonged, this prolongation is usually associated with a significant degree of pulmonary emphysema, but the degree of severity of the process cannot be determined from the spirogram tracings (Fig. 1). During an asthmatic attack there is no correlation of maximal breathing capacity with the degree of emphysema, because of the severe bronchospasm present during the seizure. The spirogram tracings in emphysema characteristically reveal a prolonged exhalation time and evidences of air trapping after a few deep breaths in rapid succession, as during the maximal breathing capacity test. This test involves rapid voluntary respiratory movements, and therefore the lungs are kept filled with more air than normal (high inspiratory level). The resultant elevation in the tracing of the rate and depth of breathing on the drum, indicates increased breathing resistance (Fig. 1).

Ratio of residual air to total lung capacity. In severe emphysema the increased residual volume in relation to total lung capacity is accompanied by impaired alveolar aeration, which increases the dead-space air and decreases lung ventilation efficiency, as measured by: the concentration of alveolar nitrogen after oxygen breathing, the percentage of oxygen extracted from the inspired air, the inspired-alveolar pO_2 difference, and the arterial pCO_2 as determined by direct tension (Table 1).

Distribution of inspired air. Since the timed vital capacity for three seconds and the maximal breathing capacity are markedly reduced in severe emphysema (Table 1), compensatory hyperventilation is limited. Thus the distribution of air from each inspired breath to all the ventilated and perfused alveoli, in proportions sufficient to supply oxygen and eliminate carbon dioxide, becomes a problem. Hyperventilation is the available compensatory respiratory mechanism. This may be adequate at rest if the emphysema is not too severe, but with exercise the hyperventilation is frequently inadequate to provide the uniform alveolar aeration required for the increased gas exchange of oxygen and carbon dioxide in the presence of an increased cardiac output from the right heart and

TABLE 1

*Comparison of Average Pulmonary Function Measurements in 50 Cases of Non-emphysema and in 50 Cases of Severe Emphysema**

	Non-emphysema	Emphysema
Age (yrs.)—avge. and range	42.3 (17–70)	55.7 (17–74)
Total vital capacity (ml.)		
Observed	4,174	2311
% of predicted	97.3	58.8
Timed vital capacity, 3-sec., (ml.)		
Observed	3,885	1502
% of predicted	90.6	38.2
Maximal breathing capacity (L./min.)		
Observed	126.0	35.7
% of predicted	88.1	30.4
Alveolar N_2 after 7 min. of breathing O_2 (%)	1.36	4.85
Residual air capacity (ml.)		
Observed	1225	2960
% of predicted	90.9	215.8
Total lung capacity (ml.)		
Observed	5,399	5271
% of predicted	95.8	99.4
Residual air capacity (% of tot. lung capacity)	22.7	56.2
Ventilation factors (% of normal predicted)	94.0	38.9
Arterial blood oxygen saturation (%)		
Rest	94.4	90.0
Exercise	93.6	86.0
Arterial blood CO_2 content (vol. %)		
Rest	45.20	51.10
Exercise	43.00	50.03
Arterial pH (glass electrode)		
Rest	7.47	7.45
Exercise	7.44	7.43
Direct resting arterial tensions (mm. Hg)		
pCO_2	36.2	46.0
pO_2	80.9	67.0
Gradients, pO_2 (mm. Hg)		
Inspired-alveolar difference	43.2	55.0
Alveolar-arterial difference	22.9	25.0
Tidal volume (ml.)		
Rest	451	416
Exercise	935	607
Ventilation (L./min./sq. M./ body surf.)		
Rest	3.90	4.13
Exercise	11.69	9.63
Oxygen uptake (ml./min./sq. M./body surf.)		
Rest	133	131
Exercise	543	371
Oxygen extracted from inspired air breathed (%)		
Rest	3.60	3.25
Exercise	4.71	3.89

* The 2 groups were selected on the basis of the percentage the residual air comprised of total lung capacity, regardless of etiology. Non-emphysema—residual air 27% or less of total lung capacity in all cases. Severe emphysema—residual air 49% or more of total lung capacity in all cases. Some of the non-emphysema subjects had functional impairment but emphysema was not a factor.

increased pulmonary blood flow. All degrees of bronchospasm may be encountered in pulmonary emphysema, as accurately demonstrated by measurements of the maximal breathing capacity before and after a treatment with a potent bronchodilator substance (such as Isuprel or Vaponefrin) administered by intermittent positive pressure breathing (6). Exercise may aggravate the bronchospasm and further hamper the uniformity of alveolar aeration. Bronchospasm along with infection constitutes an important etiologic factor in the development and progression of emphysema, and the presence of these conditions is an indication for effective bronchodilator treatment.

Pulmonary blood flow. The prolonged overinflation of the lungs results in rupture of individual alveoli, loss of lung elasticity, and the formation of varying degrees and patterns of fibrosis. There is a decrease in effective pulmonary perfusion, produced by a reduction in the number of functional pulmonary capillaries in the pulmonary vascular bed and an increase in the pulmonary vascular resistance from the elevated pulmonary artery pressure at rest, during exercise, or both (7, 8). The patient with pulmonary emphysema has difficulty increasing the pulmonary blood flow during exercise in a volume proportionate to the degree of activity, by virtue of the increased pulmonary vascular resistance in the lung and the lack of expansibility of the pulmonary bed. In order to transport a sufficient quantity of oxygen for use during exercise, the pulmonary blood flow must be increased, as well as the minute alveolar ventilation. Inability to increase the pulmonary blood flow during exercise is a characteristic finding of pulmonary emphysema and the decreased oxygen uptake is readily demonstrated, employing the one-minute step-up exercise test (thirty steps on an eight-inch stool) (9) (Table 1). A decreased minute ventilation corresponding to the exercise given may be partly the cause of the low oxygen uptake, but much more often the inadequate blood flow is the primary factor.

Ventilation factor. At sea-level pressures there is a normal difference of about 50 mm. of Hg between the mean inspired (150 mm.) and the alveolar pO_2 (100 mm.), with ventilation volumes in the range of 2.6–3.8 liters per minute per square meter of body surface. In pulmonary emphysema the mean difference between inspired and alveolar pO_2 is increased, as measured by direct determinations of the arterial pO_2 and pCO_2 and using the arterial blood to integrate all the functioning alveoli (Table 1). In some cases of emphysema the hyperventilation (as measured by the minute ventilation volume) may be adequate to maintain the regular sea-level difference and provide a normal mean alveolar pO_2 of 100 mm. of Hg. The mean inspired-alveolar pO_2 difference was well correlated with the ventilation factor in a large series of cases (Fig. 2). The ventilation factor on a percentage basis provides an approximation of the efficiency of the lungs as a bellows, and the value is determined from the average of three measurements, all expressed as a percentage of the normal predicted value, namely: the three-second timed vital capacity, the maximal breathing capacity, and the residual air capacity as a percentage of total lung capacity. Although the arterial pCO_2 level may be elevated in emphysema, the arterial pH is usually in the normal range, in the absence of cardiac failure or respiratory depression from

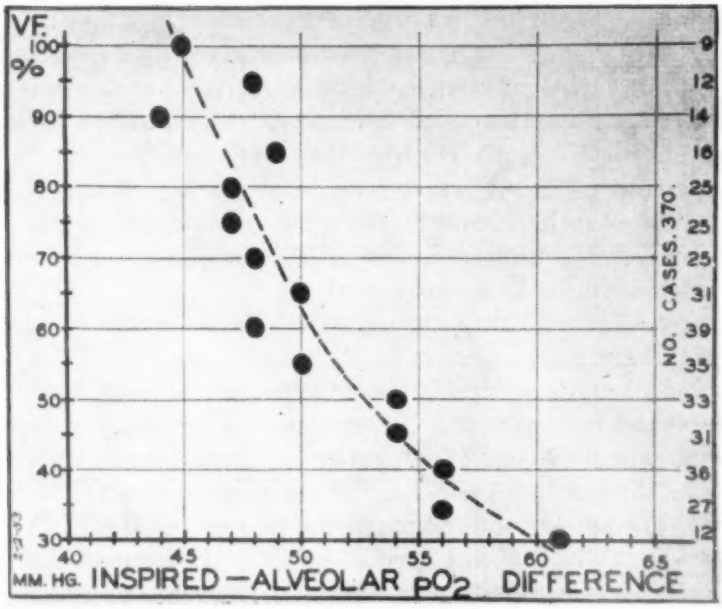

FIG. 2. Correlation between the inspired-alveolar pO_2 difference during rest and the ventilation factor. The number of cases in each group is given by the figures on the right ordinate. The 15 groups were based on the ventilation factor percentage, with step decreases of 5 per cent from 100 to 30. For example, 33 cases are listed with a ventilation factor of 50 per cent; this includes all cases with a range from 47.51 to 52.5 per cent. The normal inspired-alveolar pO_2 difference at sea level is 50 mm. of Hg. The group of patients with severe emphysema and ventilation factors less than 50 per cent had, on the average, inspired-alveolar pO_2 differences greater than 50 mm. of Hg, indicating inability to maintain normal alveolar pO_2 levels even at sea level while breathing air.

drugs, anesthetics, infections, or other acute changes (Table 1). The arterial pCO_2 is a function of alveolar aeration, and the direct measurement of arterial pCO_2 is well correlated with the ventilation factor (9).

Arterial blood O_2 saturation. Studies of the arterial blood oxygen saturation at basal rest (Van Slyke method) revealed variable saturation values in emphysema—normal in some cases but 90 per cent or more in other cases (Table 1). Using the one-minute step-up test or a steady state of treadmill exercise after ten minutes, the oxygen saturation tends to decrease below the resting level, but in some cases of emphysema there may be no decrease and in others even an increase. The saturation of the blood perfusing the lung during exercise may not be decreased, even though there is a marked decrease in oxygen uptake. This indicates an inadequate pulmonary blood flow during the exercise, although the blood that gets through comes in contact with aerated alveoli. Unequal alveolar aeration and perfusion, the distribution factor, has been found to be the main cause of the decreased arterial blood oxygen saturation observed in emphysema. Some alveoli are poorly aerated, yet they are perfused either normally or with a decreased amount of blood; other alveoli are perfused but not aerated (actually representing a small shunt); and some alveoli are ventilated but not perfused,

TABLE 2

Comparison of Ambient Breathing of Compressed Air with Intermittent Positive-Pressure Breathing (IPPB) of Compressed Air, in a Patient with Severe Emphysema

Type of breathing	Ambient (compressed air)	IPPB (compressed air; no bronchodilator)
Resp. rate/min	12.7	5.3
Ventilation (L./min./sq. M./body surf.)	3.62	3.07
Tidal air (ml.)	479	972
Arterial O_2 sat. at rest (%)	91.6	94.6
Arterial pCO_2 (mm. Hg)	47.0	40.0
Alveolar pO_2 (mm. Hg)	91.0	101.0
Arterial pO_2 (mm. Hg)	67.0	85.0
Alv.-art. pO_2 difference (mm. Hg)	24.0	16.0
Effective tidal air (%)	53.0	60.0

thereby decreasing the lung ventilation efficiency because of the increased dead space. In this laboratory, diffusion difficulty (increased resistance in the pulmonary membrane) has not been a significant factor in the unsaturation of the blood observed in pulmonary emphysema. Intermittent positive-pressure breathing with compressed air restores the blood saturation almost to a normal level in many cases of emphysema, by improving the ventilation in the poorly aerated alveoli. In Table 2 the results are compared to those obtained during ambient breathing. A similar mechanism produces the improvement noted during exercise, *i.e.*, more uniform alveolar aeration with the deeper breathing. Shunting of blood through nonventilated areas, with resulting arterial unsaturation, cannot be improved by the ventilatory approach; it may possibly involve some reversal of flow through the bronchial pulmonary artery anastomosis.

Minute ventilation volume. In emphysema the minute ventilation volume is frequently increased, both at rest and with exercise (compensatory hyperventilation). A decreased minute ventilation during exercise indicates an inadequate bellows action of the chest and lungs. The basal resting oxygen uptake is normal in pulmonary emphysema and shows no correlation with the ratio of residual air to total lung capacity. The oxygen uptake during exercise is decreased in pulmonary emphysema. This measurement is well correlated with the severity of the emphysema and is indirectly an indication of the presence of an increased pulmonary vascular resistance (Table 1). The lung ventilation efficiency is decreased in pulmonary emphysema, as measured by the percentage of oxygen extracted from the inspired air breathed both at rest and during exercise. To obtain sufficient oxygen, the subject has to breathe more than the normal amount of air.

Blood volume and circulation time. The ether circulation time (arm to lung) and the decholin circulation time (arm to tongue) have been found to show no correlation with the degree of pulmonary emphysema, based on residual air measurements. Hemoglobin determinations (Van Slyke oxygen capacity), the hematocrit, and the blood volume (T-1824 dye, using arterial blood) have been found to show no correlation with the degree of emphysema per se in the absence of cardiac failure. Prolongation of the ether or decholin circulation times, or a

significant increase in blood volume, hematocrit, or hemoglobin usually indicates the presence of cardiac factors as part of the clinical picture (10).

INTERMITTENT POSITIVE-PRESSURE BREATHING (IPPB)

Clinical observations and studies have been performed over an extended period of time, employing intermittent positive-pressure breathing (IPPB) ~~of compressed air~~ combined with simultaneous nebulization of a bronchodilator substance in the management of chronic pulmonary disease (6, 11). The IPPB method of treatment is very satisfactory for providing subjective relief in many types of chronic pulmonary ailments with associated fibrosis and emphysema. It should be regarded as a useful procedure to be used in conjunction with any other indicated therapy. Although it was first developed in the treatment of coal miners' silicosis with fibrosis and pulmonary emphysema (11), it has been found helpful in many other varieties of emphysema, regardless of the etiology.

This new type of therapy is fundamentally directed at rehabilitation of the remaining ventilated and perfused lung tissue, by providing improved alveolar aeration to those parts of the lungs poorly ventilated on ambient breathing, particularly the bases. The lungs are actively inflated by means of a regulated safe positive pressure during inspiration (the maximal pressure employed varies from 15 to 20 cm. of water), after which the lungs passively become deflated to atmospheric pressure during expiration, principally because of the elastic recoil of the lungs and chest-wall structures. The apparatus is designed to follow the patient's pattern of breathing. Physiologic studies indicate that IPPB improves the depth of breathing, provides better excursions of the diaphragm, and often maintains a more uniform alveolar aeration, as compared to the individuals' ambient breathing (12). Thus the nature of the physiologic disturbance may be revealed. IPPB provides a more uniform distribution of aerosol in the lungs when the bronchodilator is nebulized and administered simultaneously, especially at the bases in cases of far advanced emphysema (Table 3). Antibiotics, detergents, proteolytic and wetting agents may also be administered in this manner. The IPPB method provides for the maximal beneficial response from the aerosol used, particularly in the emphysema patient, because of the more uniform distribution to all parts of the lungs when the breathing resistance is markedly increased (Table 3). The improvement observed in the gas exchange during exercise in some cases results from deeper breathing and hence more uniform alveolar aeration as compared to the resting status. The arterial blood oxygen saturation was increased in 78 out of 122 coal miners during a steady state of mild to moderate treadmill exercise, the average saturation being 92.0 per cent at rest and 94.1 per cent after ten minutes of treadmill exercise.

Mucus and secretions are not pushed farther down the respiratory tract by IPPB; in fact, bronchial drainage is enhanced by the rhythmic inflation and deflation of the lungs in a manner similar to the mechanics by which a cough raises secretions. This expectorant-like feature of IPPB has been very helpful both in the preoperative treatment of bronchiectasis in patients suitable for chest surgery and in the nonoperative management of patients unsuitable for chest

TABLE 3

Comparison of Effectiveness of Administration of Bronchodilator by Hand Nebulizer and Intermittent Positive-Pressure Breathing (IPPB), in a Patient with Severe Emphysema

Type of breathing	Isuprel by hand nebulizer (ambient, with compressed air)	IPPB (compressed air; no bronchodilator)	Isuprel by IPPB with compressed air
Resp. rate/min.	12.0	8.7	10.0
Ventilation (L./min./sq. M./body surf.)	2.91	2.68	4.79
Tidal air (ml.)	364	462	719
Arterial O_2 sat. at rest (%)	88.5	94.7	97.2
Arterial pCO_2 (mm. Hg)	51	44	43
Alveolar pO_2 (mm. Hg)	86	95	104
Arterial pO_2 (mm. Hg)	62	73	84
Alv.-art. pO_2 difference (mm. Hg)	24	22	20
Effective tidal air (%)	60	57	73

surgery (13). The effectiveness of the IPPB treatments in promoting bronchial drainage may be enhanced in some instances by putting the patient in a slight Trendelenburg position. The secretions are usually not completely eliminated by IPPB in bronchiectasis, but in most cases there is a significant reduction in the amount of sputum after a week to ten days of daily treatments with a suitable bronchodilator drug (such as Isuprel and Vaponefrin). A short course of IPPB treatments for seven to ten days is often very helpful in preparing some of the poor-risk patients for surgery.

IPPB provides an involuntary, periodic and effective regulated breathing exercise which, when taken daily over an extended period of time, tends to improve muscle tone. Many patients with severe emphysema are unable to obtain the benefits of an effective breathing exercise because of the impaired movement of the diaphragm, the increased breathing resistance and the inadequate minute volume of ventilation. The IPPB method tends to insure better cooperation for obtaining regularly effective breathing exercise on the part of the patient. With the use of an apparatus the exercise is more apt to be routine, and moreover it is very easy to breathe, since most of the work is performed by the apparatus when the subject relaxes.

Long-range study. Since pulmonary emphysema tends to be a slowly progressive condition, a long-range study was desirable in order to provide quantitative data on the condition by serial measurements of the residual air volume in patients receiving daily treatment with IPPB. In Table 4 are given objective physiologic measurements in 11 patients with pulmonary emphysema who received daily IPPB treatments at home for several months (three to thirty-six), employing their own individual pressure breathing units (Table 4). The residual air capacity was increased to a significant degree in only 2 of the 11 patients followed—in one after three months of treatment and in the other after thirteen months. There was a significant decrease in the absolute value of the residual air in 7 patients and no significant change in 2. In 7 of the 11 patients there was

TABLE 4

Study of the Effects of Prolonged Intermittent Positive-Pressure Breathing Treatments with Bronchodilators in Pulmonary Emphysema

Case	Age (yrs.)	Duration of treatment (mos.)	Supine vital capacity (ml.)		Residual air capacity (ml.)		Residual, as % of tot. lung capacity		Ventilation factor (%)		Alveolar nitrogen (%)	
			Before	After	Before	After	Before	After	Before	After	Before	After
1	62	3	3,910	4,070	4,153	3,982	51.5	49.5	41.1	41.9	4.91	6.71
2	75	3	2,440	2,320	2,701	3,395	52.5	59.4	35.4	35.9	7.68	6.59
3	62	9	2,260	2,970	3,651	3,252	61.8	52.3	33.8	37.5	5.57	3.14
4	66	9.5	2,040	1,750	3,792	3,365	65.0	65.8	29.1	28.6	7.09	9.13
5	63	11	2,350	3,095	4,371	3,019	65.0	49.4	35.3	42.4	6.76	4.52
6	64	12	3,020	3,300	2,404	2,028	44.3	38.1	50.9	54.7	2.94	3.27
7	64	13	4,020	3,500	3,283	2,760	45.0	44.1	38.8	43.3	6.97	4.21
8	61	13	1,900	1,925	2,492	2,811	56.7	59.4	28.0	28.5	7.52	7.02
9	56	22	2,780	3,060	3,188	3,209	53.4	51.2	34.9	—	3.21	2.11
10	58	32	1,488	1,700	3,502	2,867	70.2	62.8	25.3	29.4	9.18	3.42
11	44	36	1,860	2,340	2,913	2,192	61.0	48.4	27.3	32.8	8.09	3.96

a slight improvement in the pulmonary emphysema, on the basis of quantitative measurements of the residual air and the ratio of the residual air to total lung capacity. These data suggest that in some cases of severe emphysema, if IPPB be administered daily, a further increase in residual air may be prevented. Although the number of cases with follow-up studies is small, the information thus far appears to provide encouragement for the premise that the proper use of IPPB with a bronchodilator may check emphysema, which otherwise characteristically tends to be progressive. In the 11 cases presented, there was no history of dust exposure and the etiology of the emphysema was unknown except for 1 case of pulmonary tuberculosis. A history of past attacks of pneumonia and frequent colds was common in this group. Bronchospasm and infection appear to be two outstanding factors in the etiology of pulmonary emphysema in the absence of known specific agents.

The chief defect in pulmonary emphysema is the increased resistance to breathing which affects the ability of the patient to move air in and out of the lungs in adequate volumes, especially during increased activity. The marked decrease in the ventilation factor characteristic of severe pulmonary emphysema (Table 1) reflects this state of increased breathing resistance. In all of the cases except 1, when the residual air was significantly decreased after the IPPB treatments (Table 4), there was also a slight increase in the ventilation factor. The pathologic changes which produce emphysema by increasing the ratio of residual air to total lung capacity are characteristically accompanied by simultaneous decreases in the three-second vital capacity and the maximal breathing capacity. In 5 of the 7 patients showing a decrease in the residual air capacity, the alveolar nitrogen after breathing oxygen for seven minutes was also significantly decreased. The alveolar nitrogen percentage is an index of the uniformity of air distribution in the lung, and normally this should not exceed 1.5 per cent after

breathing oxygen for seven minutes (3). In 5 of the patients with a decreased residual capacity after IPPB, the vital capacity was significantly increased, and in 1 patient (No. 7) there was a decrease in the vital capacity of 520 ml. and an increase in the residual air of 523 ml.

In the group of 11 patients described in Table 4, all but 1 were over 55 years of age, and all were totally disabled as appraised by the results of a complete set of pulmonary function measurements. This group was characteristic of patients with severe emphysema who seek treatment. Numerous observations have been made on the effectiveness of the IPPB procedure in chronic pulmonary disease, based primarily on clinical observations and in some instances supplemented by data from spirogram recordings before and after treatment (13–17). One report has been published which questions the superiority of the IPPB method of bronchodilator administration in emphysema (18); however, the data were based on a small series of cases over a short observation period and no evidence was presented to show that exactly the same amount of bronchodilator drug was administered in the control group of cases. Spirogram recordings taken before and after short periods of treatment (one treatment, or a course extending over two or three weeks) generally indicate only the degree of bronchospasm which may exist. Patients with severe bronchospasm usually have a rapid subjective response to IPPB with a bronchodilator. In emphysema, however, the clinical response to IPPB may be slow, and several months of daily treatments may be required in order to obtain a clearly defined beneficial effect in the severe case. Most of these patients who seek relief have had their slowly progressive disease for many years, and usually they have received the commonly recommended treatments for emphysema, such as bronchodilators (administered by hand nebulization or other devices which depend on the patient's own inspiratory effort to get the drug into the lungs and bronchioles), digitalis, aminophyllin, mercurial diuretics, cortisone, dietary restrictions, low-sodium intake and other procedures. Following the addition of IPPB to the foregoing forms of treatment there is significant clinical improvement. Fluids and expectorants are frequently helpful as supplements. In a sense, each patient serves as a control; the same doctor, who is usually well acquainted with the patient, makes the clinical observations before and after the IPPB treatments.

Helium. The use of 60 per cent helium and 40 per cent oxygen when administering IPPB and bronchodilators facilitates the transfer of oxygen around secretions and the relief of bronchospasm in the bronchioles. The highly diffusible helium helps to carry the gas and bronchodilator substance to the site of the spasm and obstruction in the bronchioles. Thus, there is more effective treatment of the bronchospasm, and the movement of air beyond the secretions in the bronchioles enables the patient to expectorate more effectively. This use of helium has been of great advantage in cases with severe emphysema and marked plugging of the bronchioles from a pulmonary infection, aggravated by bronchospasm; status asthmaticus may be markedly benefited. If cortisone is used, a suitable antibiotic should be given simultaneously in order to combat infection.

Oxygen can be administered with the IPPB apparatus without danger of CO_2

retention in even the most severe cases of pulmonary emphysema, as has been repeatedly demonstrated in this laboratory by comparing arterial pCO_2, pH, and CO_2 content during ambient air breathing and during IPPB with 99.6 per cent oxygen. Recent studies in a case of suspected oxygen toxicity from IPPB treatments revealed that the patient had an arterial CO_2 content of 56.35 volumes per cent when breathing air at ambient pressure; but after ten minutes of IPPB with oxygen (no bronchodilator), the CO_2 content was reduced to 52.75 volumes per cent—a decrease of almost 4 volumes per cent.

Infection of the respiratory tract in emphysema should be managed with IPPB, bronchodilators and antibiotics as indicated. Effective treatment of the bronchospasm by the IPPB method of administration helps minimize the factors promoting the retention of secretions and impairing alveolar aeration and respiratory gas exchange. Sedatives and respiratory depressant drugs decrease minute ventilation, retard bronchial drainage, and may promote retention of CO_2 to dangerous levels; they should be avoided as far as possible. Most so called "cough" preparations containing sedatives or depressants probably do more harm than good because of the retardation of bronchial drainage and further impairment of alveolar aeration.

SUMMARY

Pulmonary function measurements in patients with pulmonary emphysema show that 1) the main difficulty is the increased resistance to moving air in and out of the lungs, and 2) the most characteristic abnormality in blood gas exchange is unequal alveolar aeration and perfusion. Impaired diffusion across the pulmonary membrane is seldom present.

Intermittent positive-pressure breathing ~~of compressed air~~ (IPPB) along with suitable bronchodilators is a valuable therapeutic procedure in the treatment of pulmonary emphysema, in association with other routine measures. The increase in activity observed in patients following treatment with IPPB can serve as a clinical index of improvement when facilities are not available for more precise quantitative measurements of pulmonary function. IPPB provides relief and control of symptoms in most cases of emphysema with dyspnea. Early observations based on follow-up quantitative measurements of residual air after many months of continuous daily IPPB indicate that this type of therapy may prevent the progression of emphysema. IPPB is a method of treatment and not a cure. Normal lung condition is not restored. However, if the progression of emphysema can be halted, this in itself is a most valuable therapeutic application.

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INTRATHORACIC SURGICAL PROCEDURES IN PATIENTS PAST THE AGE OF 60*

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Increased longevity, coupled with the increased incidence of bronchogenic carcinoma has resulted in the necessity for considering thoracotomy and pulmonary resection in an expanding segment of the population. The over-all safety as well as the feasibility of well-ordered thoracotomy is established but little specific attention has been directed to its performance in the later decades of life, even though numerous studies have been made of the results of general surgical operations in the aged. One might well expect that elderly patients subjected to thoracic surgical procedures would do well as a group, since all investigators seem to agree that high mortality rates in such persons are encountered only in those undergoing emergency operations, or in those who are in poor states of hydration or nutritional balance. These adverse situations are uncommon in thoracic diseases amenable to surgical treatment.

In an effort to adjudge the risk of thoracotomy and pulmonary resection in elderly people, we have analyzed our recent experiences. The results of this analysis and some of our reactions to the problems involved are presented here.

CLINICAL STUDIES

Clinical material

In the period between July 1, 1952 and May 1, 1954, 31 patients 60 years of age or older were subjected to thoracotomy. The indication in all of them was known or suspected malignancy.

Table 1 shows the lesions actually found at operation. They were predominantly malignant in nature. Table 2 lists the surgical procedures carried out. In general, it may be seen that we were less radical in the older age group, preferring to perform the simplest adequate procedure. The circumstances attendant upon the 2 fatalities are of interest and are given briefly:

L. B., a 65-year-old white male, was admitted because of possible tuberculosis. Diagnostic procedures failed to reveal any evidence of tuberculosis. Instead, the patient was found to have a bronchogenic carcinoma. Thoracotomy was performed. During attempts to dissect

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TABLE 1

Primary Diagnosis

I. *Malignant*		23
A. Bronchogenic carcinoma	19	
B. Sarcoma	2	
C. Metastatic tumors	1	
D. Tuberculoma and malignancy (primary or secondary not differentiated)	1	
II. *Benign*		8
A. Abscess	3	
B. Benign tumors	2	
C. Other benign process	3	

TABLE 2

Operation	No.	Deaths
Exploration and biopsy	8	1
Exploration and wedge-excision or enucleation	2	0
Lobectomy	9	0
Thoracotomy and decortication	1	0
Thoracotomy and drainage	1	0
Bi-segmental resection	2	0
Bi-lobectomy	2	0
Pneumonectomy	5	1
Pleuropneumonectomy	1	0
	31	*2*

the hilum, a tear in the right pulmonary artery occurred. It was necessary to ligate this vessel, even though a pneumonectomy was technically impossible. The patient died on the fifth postoperative day from respiratory insufficiency. He was a known cardiac.

H. M., a 61-year-old white male, was operated upon for a squamous-cell carcinoma of the right upper lobe. The patient was placed in the lateral decubitus position. Considerable secretion escaped from the suppurating upper lobe and flooded the left lung. These secretions were aspirated from the left bronchus and the airway was believed to have been cleared. Seven minutes after ligation of the right pulmonary artery, however, the patient's heart stopped and he could not be revived. The facts in this case showed that the left lung had not been adequately cleared and death ensued when he was deprived of the use of the right, middle and lower lobes by ligation of the right pulmonary artery.

Effect of cardiac disease

In Table 3 an attempt has been made to assess the risk of known cardiac disease. Its presence is not a contraindication to surgical therapy, provided compensation is good. If digitalis is used, the cardiac failure must be well controlled by the drug. We do not consider it necessary to administer digitalis routinely before operation in the absence of cardiac failure. If cardiac failure occurs postoperatively, it can be recognized by persistent dyspnea, persistent rales in the bases of the lung, and by the presence of a tender liver. Dependent edema is not a usual feature of postoperative cardiac failure. Rapid digitalization is accom-

TABLE 3

Cardiac Status

	No. of Cases	Death	Post op. cardiac failure
Arteriosclerotic heart disease	5	1	2
Old myocardial infarction	2	0	0
Aortic insufficiency and aneurysm (mild CVA)	1	0	1
Rheumatic aortic stenosis	1	0	1
	–	–	–
	9	*1*	*4*

TABLE 4

Electrocardiographic Findings

	No. of Cases	Death
Normal	8	1
Probably normal	11	1
Abnormal	12	0
	—	–
	31	*2*

plished by either intravenous or oral administration, depending upon the urgency of the situation. Abnormal electrocardiographic findings were not correlated with either increased morbidity or mortality in our study, as suggested by the data in Table 4.

As Gross *et al.* (1) have pointed out, cardiac disease is usually not the cause of death in elderly patients undergoing surgical operations. As an index of cardiac and respiratory reserve, we routinely employ the ancient test of climbing two flights of stairs, and consider a patient to be an acceptable surgical risk if he can perform this exercise without dyspnea or pain. As shown in Table 3, arteriosclerotic heart disease appears to be a more serious cardiac problem postoperatively than is an old infarction of the myocardium. This is understandable, since arteriosclerotic heart disease is a diffuse process affecting both ventricles, whereas coronary occlusion is predominantly a disease of the left ventricle. Pulmonary resection, particularly pneumonectomy, involves strain on the right heart rather than on the left; therefore, a coronary occlusion which is not fresh need not increase the risk of surgery prohibitively.

Influence of mental status

The mental status of our patients has been of interest. It is our distinct impression that patients who display little mental inertia generally respond well to surgical therapy, whereas those who are just content to "sit and rock," do not. It is important that the patient have something to live for and that he be interested in continuing his existence; also that he be optimistic as to the outcome and not unduly fearful. Operation has usually not been withheld because of an

adverse mental attitude; nevertheless, a favorable mental outlook is very desirable.

Blood volume

Several investigators have stressed the fact that blood volume studies are of great importance in the preoperative study of elderly patients undergoing operation (2, 3, 4). We do not make blood volume determinations, but rely solely on the clinical appearance of the patient as a criterion for preoperative blood replacement. Blood volume studies are probably of greater importance in those patients in whom dehydration is a problem. However, at times the usual laboratory measurements such as hematocrit, hemoglobin and plasma protein concentration can be deceiving.

Associated diseases

Patients in the age bracket under consideration often have concomitant diseases that complicate management. Two of our patients required other major surgical procedures prior to their thoracic surgical operations. One was admitted with a ruptured duodenal ulcer which necessitated closure. The other had acute suppurative appendicitis with perforation while in the hospital being processed prior to his thoracic operation. Both of these patients recovered without incident after the abdominal operations. Excluding those with heart disease, there were 9 patients who were found to have some other condition in addition to their thoracic disease. These conditions included asthma, syphilis, gout, cholelithiasis, benign prostatic hypertrophy, urethral stricture, inguinal hernia and cirrhosis. No relevant complications were encountered in any of this group.

Postoperative care

Care during the time of operation and in the immediate postoperative period is obviously of vital concern. Blood replacement is essential. However, it must be remembered that an elderly person's circulatory system cannot stand abuse as readily as that of a younger person. Shock on the one hand and circulatory overload on the other, must be avoided. We use the gravimetric method for determining the blood absorbed by sponges, and measure the loss due to suction directly in the operating room. This provides a means of estimating blood loss, to be used as a guide to proper replacement of blood as the loss occurs. Fluids and electrolytes are doled out in an especially frugal manner, to prevent pulmonary edema. This is especially true following pneumonectomies. Postoperatively, it is better to err on the side of slight dehydration and slight chloride deficiency. Fortunately, most of our patients are able to take fluids by mouth within six to twelve hours after operation, and so avoid the dangers of prolonged intravenous therapy during the postoperative phase. From 1,500 to 2,000 cc. of fluid intake on the day of operation is generally adequate.

It is not necessary that large quantities of urine be excreted during the postoperative phase. If the patient excretes 500 cc. per day for the first two to three days, this is considered an adequate quantity and no attempt is made to force fluids orally or to administer them intravenously.

TABLE 5

Operation	Non-fatal complications	Outcome
1. Rt. upper lobe and rt. middle lobectomy	Postoperative shock	Responded to 500 cc. blood transfusion
2. Rt. lower lobectomy	Thrombophlebitis, left leg	Recovered with anticoagulants
3. Resection, apical posterior segment, left upper lobe; and superior segment, lower lobe	Bronchopleural fistula and empyema	Recovered after drainage
4. Rt. upper lobectomy	* Cardiac arrhythmia; mild CVA 5th day	Recovered without residuals
5. Rt. upper lobe and rt. middle lobectomy	Atelectasis	Recovered after repeated bronchoscopy
6. Pneumonectomy (known cardiac)	Penicillin reaction	Recovered
	* Cardiac failure	Recovered
7. Rt. upper lobectomy	* Cardiac failure	Recovered
8. Rt. lower lobectomy	Subcutaneous emphysema	Recovered
9. Enucleation of rt. lower lobe lesion	Delayed pneumothorax, two weeks postoperatively	Water-seal drainage; recovered
10. Rt. lower lobectomy	* Cardiac failure	Recovered
11. Exploratory thoracotomy & biopsy	Gastric hemorrhage from peptic ulcer	Responded to nonoperative measures

* Included in Table 3.

Morbidity

In an attempt to evaluate morbidity, all complications (excluding the 2 deaths) were studied and are listed in Table 5. Most of these complications were readily handled. Except for the occurrence of cardiac failure in association with clinical heart disease prior to operation, the complications were no more unusual than those ordinarily encountered in the practice of thoracic surgery.

In Case 1, the patient was in a state of mild shock postoperatively, which was due to insufficient blood replacement in the operating room. In this instance, the anesthetist failed to replace blood as it was lost, because of the fear of overloading the circulatory system. A transfusion of 500 cc. of blood restored the patient's circulatory dynamics to normal and he made an uneventful recovery.

In Case 2, a mild thrombophlebitis occurred in the left lower extremity, following the insertion of a # 15-gauge needle into the saphenous vein at operation, for the replacement of blood and fluids. This patient responded satisfactorily to anticoagulants.

In Case 3 a bronchopleural fistula and empyema developed, which required intercostal drainage.

In Case 4 there was auricular fibrillation in the postoperative phase. Medical consultation was sought, but the rhythm reverted to normal before the medical resident could get to the recovery room. An electrocardiogram obtained during the attack demonstrated the nature of the arrhythmia. This patient also had a mild and transient cerebrovascular accident on the fifth postoperative day. The

clinical evidence lasted only a few hours, and he recovered without residual signs. The frequently transient nature of postoperative auricular fibrillation and other arrhythmias is illustrated by this case.

In Case 5 atelectasis occurred because of the patient's unwillingness to cough. He had to be bronchoscoped daily for several days, but otherwise recovered without further difficulty.

In Case 6, pneumonectomy was performed in a known cardiac who was also hypersensitive to penicillin. We chose to administer penicillin postoperatively to this patient because we had as yet not been impressed by the dependability of broad-spectrum antibiotics employed prophylactically. The patient had a reaction to penicillin, but it was controlled by antihistaminics. Cardiac failure also developed approximately two weeks postoperatively and this again responded to digitalization.

In Case 7 a right upper lobectomy was performed. The patient was a known cardiac with rheumatic aortic stenosis, and cardiac failure developed postoperatively. This was controlled by digitalis.

In Case 8 subcutaneous emphysema occurred after a right lower lobectomy. The mechanism has not been explained. The two intercostal water-seal tubes employed for drainage were working well. However, the emphysema disappeared in a few days.

In Case 9, the patient had an enucleation of a small rounded lesion in the right lower lobe and was convalescing smoothly until two weeks postoperatively, at which time a spontaneous pneumothorax developed on the right side. Water-seal drainage was employed, using an intercostal catheter. Recovery was uneventful.

In Case 10 cardiac failure developed postoperatively. The patient was known to have arteriosIcerotic heart disease, and he responded well to digitalization.

In Case 11 the patient underwent an exploratory thoracotomy and biopsy of an inoperable lung tumor. While receiving deep x-ray therapy, he had a gastric hemorrhage from a peptic ulcer. This responded to the usual conservative measures.

SUMMARY

In a recent unselected group of 31 patients who were 60 years of age or older, major intrathoracic surgical operations were carried out with gratifying success. These operations were performed for known or suspected malignant conditions. In 23 of the 31 patients, the presence of malignancy was confirmed.

Definitive surgical procedures were carried out in all but 8 instances, and included all degrees of pulmonary resection. In the older patients there was a tendency to use lobectomy for removal of tumors, but pneumonectomy was performed in 6 instances.

There were 2 deaths in the entire series. One occurred as the result of a technical accident in an otherwise unmanageable situation. The other resulted from flooding of the contralateral lung by heavy bronchial secretions during the preliminary stages of a proposed pneumonectomy for carcinoma.

There were 11 postoperative complications of all types, but only 4 were directly surgical. Only 1 of these (empyema and bronchopleural fistula) could be considered to add significantly to morbidity; the other 3 were recurrent atelectasis, moderate subcutaneous emphysema and a pneumothorax occurring spontaneously late in the postoperative period.

Of 9 patients with known cardiac disease, only 4 suffered from failure postoperatively. These 4 responded to appropriate therapy, and cardiac disease was not adjudged responsible for either of the deaths recorded.

We have been impressed by the fact that the elderly patient can undergo extensive intrathoracic surgery. Favorable prognostic signs are: 1) good performance in simple work tests, and 2) mental alertness, in a patient who manifests a will to survive and gives evidence that he can accept the discomfort and inconvenience of operation in return for the prospect of prolonged life.

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THE CLINICAL EVALUATION OF METICORTEN IN RHEUMATOID ARTHRITIS AND ALLIED CONDITIONS

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Meticorten (metacortandracin)[1], a new synthetic steroid, was subjected to clinical trial and metabolic study by Bunim, Pechet and Bollet at the National Institute of Arthritis and Metabolic Diseases. Their report was read at the Interim Session of the American Rheumatism Association, Bethesda, Maryland, November 4, 1954, and the article was published in the Journal of the American Medical Association (1).

We followed Dr. Bunim's plan of treatment for the most part. Our investigational studies began November 27, 1954. Fifty-seven patients were observed, as shown in Table 1. There were 44 cases of rheumatoid arthritis, 3 of rheumatoid spondylitis and 10 of non-rheumatoid disorders.

RHEUMATOID ARTHRITIS

In most of the cases in the rheumatoid group the disease was advanced—Stage III or IV (2). Ages of patients ranged from 31 to 64 years, and duration of the disease from one to twenty-nine years. All but 3 patients had formerly received cortisone, hydrocortisone or ACTH. Intractable cases were intentionally selected, *i.e.*, those having responded unsatisfactorily to previous treatment or having suffered undesirable reactions to cortisone or its analogues.

We discovered, fortuitously, that smaller suppressive doses of Meticorten were often as effective as larger ones. Most of our patients were started on 20 mg. daily instead of 30 mg., because they could not be observed daily and because some of them had fear complexes following severe reactions to cortisone.

The dosage schedules most successfully used by us were as follows: If the total daily requirement was 30 mg., we gave 5 mg. every three hours during the day; if 25 mg., 5 mg. every four hours during the day; if 20 mg., 5 mg. after meals and at bedtime; and if 10 mg. (maintenance), 5 mg. after breakfast and 5 mg. after the evening meal. Individual adjustments influence the size of the dose and the rate of increase or reduction in dosage. These adjustments depend on the patient's past experience with steroid therapy (including side effects), his general physical status and the manner in which he responds to Meticorten.

[1] Meticorten for this study was supplied by the Schering Corporation, Bloomfield, New Jersey.

The generic term for Meticorten during the early stages of research was "metacortandracin" and for Meticortelone, "metacortandralone." In cooperation with, and by the advice of the Council on Pharmacy and Chemistry of the American Medical Association these names have now been changed to "prednisone" (Meticorten) and "prednisolone" (Meticortelone).

Prednisone and prednisolone were subjected to rigid laboratory and pharmacological tests by the biological research staff of the Schering Corporation prior to clinical studies. The therapeutic effects of the two compounds are identical. Prednisone, under the Schering brand name of Meticorten, was used exclusively in this project.

TABLE 1

Clinical Evaluation of Meticorten in 57 Cases of Rheumatoid Arthritis and Allied Conditions

Disease	No. of cases	Stage*	No. of cases	Class**				Patients			Duration of disease (yrs.)	Previous treatment		Meticorten				
								Age	Sex					Dose (mg.)	Grade of improvement†			
				I	II	III	IV		F	M					I	II	III	IV
Rheumatoid arthritis	44	I	7	7	0	0	0	31 to 48	7	0	1 to 15	Cortisone Hydrocortisone ACTH	6 2 2	25 to 5	5	2	0	0
		II	14	2	12	0	0	31 to 64	12	2	2 to 15	Cortisone Hydrocortisone ACTH	13 8 4	40 to 15	6	5	2	1
		III	9	0	9	0	0	33 to 56	7	2	3½ to 15	Cortisone Hydrocortisone ACTH	9 5 4	30 to 10	4	4	1	0
		IV	14	0	11	2	1	35 to 64	12	2	2½ to 29	Cortisone Hydrocortisone ACTH	13 6 3	30 to 7½	3	9	2	0
Rheumatoid spondylitis	3	III	1	0	1	0	0	23	0	1	6	Cortisone Hydrocortisone	1 1	30 to 10	0	1	2	0
		IV	2	0	2	0	0	30 to 33	0	2	8 to 10	Cortisone Hydrocortisone	1 1					
				Class														
Dermatomyositis (collagen disease)	1	Moderately advanced		III				55	1	0	1	Cortisone		20 to 30	0	1	0	0

Gouty arthritis	3	Moderately advanced 1 Advanced 2	II–2 III–1	50 to 57	1	2	4 to 20	Cortisone	3	30 to 20	1	1	1	0
Osteoarthritis		All advanced		58	4	0	5	Cortisone	2	30	1	2	1	0
Knees	1		II	to			to			to				
Knees (traumatic factor)	1		II	77			15			10				
Pressure paralysis, lumbar	1		IV											
Nerve root pressure, lumbosacral	1		III											
Intractable torticollis	1	Chronic	II	60	1	0	15	Cortisone		20	1	0	0	0
Refractory bursitis	1	Subacute	III	65	0	1	3 mos.	Cortisone		30 to 15	1	0	0	0

* *Stage of Disease* (2)

I. Osteoporosis may be present, but no destructive changes.

II. Osteoporosis with or without slight cartilage destruction and muscle atrophy. There may be limited motion and extra-articular lesions.

III. Extensive atrophy. Cartilage and bone destruction. Deformities. Osteoporosis.

IV. Same as Stage III, with fibrous and bony ankylosis.

** *Class of Functional Capacity* (2)

I. Unimpaired.

II. Normal activities despite discomfort and limited motion.

III. Limited, foregoing usual occupation but caring for self.

IV. Bedridden, largely incapacitated for self care.

† *Grade of Improvement* (2)

I. Complete remission (including normal erythrocyte sedimentation rate). No signs of joint inflammation. Irreversible deformities accepted.

II. Major improvement with minimal residual joint signs.

III. Minor improvement. Decreased, but not minimal swelling. No articular or extra-articular activity in new sites

IV. Unimproved. X-ray evidence of advancing disease.

Many patients in the rheumatoid group had improved to a certain point with other treatment. However, there was still some periarticular swelling and thickening which interfered with functional capacity. Nineteen of these cases showed complete reversal, and 20 showed major improvement during Meticorten therapy. The residual signs described gradually disappeared and the restoration was maintained with minimal doses. The grade of improvement (2) was based on objective findings at the beginning of Meticorten treatment. The same workers observed the same patients, who were studied earlier in clinical research with cortisone and other steroids.

A few examples of the response in individual cases are cited.

Case 1. A man, 55 years of age, had suffered from generalized, rapidly progressive rheumatoid arthritis for four years. When first seen September 29, 1953, he was in a state of "hypercortisonism" and could hardly walk. He had taken cortisone, 100 mg. daily for eighteen months. In the beginning it was "wonderful" but gradually became ineffective until he was hospitalized October 3, 1953, for "cortisone addiction," receiving Lipo Adrenal Cortex and ACTH plus general supportive treatment and physical therapy. After leaving the hospital, corticotropin gel, alternating with moderate doses of cortisone, was administered. In general, the condition of his joints improved but there never was reversal of the swelling of the hand joints. They resembled the hands of an acromegalic patient. The fingers could not be flexed and he could hardly manage a button. One knee was swollen and flexed 15 degrees. The tempero-mandibular joints were limited in motion. Meticorten was started December 10, 1954, in a dosage of 20 mg. daily. The erythrocyte sedimentation rate (Westergren corrected) was 19 mm. in one hour. Four days later, the patient stated that after twenty-four hours the swellings "began to melt away" so that he could make a fair fist. On the seventh day he could straighten the knee and said that he felt better than he had felt in four years. The erythrocyte sedimentation rate was 7 mm. in one hour. In fourteen days the swelling of the knee had completely disappeared and the dose of Meticorten was reduced to 15 mg. daily. Twenty-one days after starting treatment, the function of the tempero-mandibular joints became normal. An interesting side light in this case was the disappearance of subcutaneous nodules, each 2 cm. in diameter, which had been present below the elbows. On the twenty-eighth day, the patient left for a prolonged rest in Florida, on a maintenance dosage of 10 mg. daily. His total dose had been 1,097 mg. Recent report of progress—"excellent".

Case 2, the first treated in our series. This patient was a man, 50 years of age, who had had progressive rheumatoid arthritis for eleven years. He had been seen three years after the onset, at which time he had presented marked joint swellings, hand deformities, knee effusion and contractures. He spent six months in the hospital for rest, intensive supportive treatment and straightening of the knees. Then, after a winter in Tucson, he returned to work and got along fairly well on maintenance gold therapy. When cortisone became available, injections, and later tablets were given. The joints of the hands and knees remained swollen and limited in motion. The knees became more and more troublesome, so that walking was difficult. In 1953, the knee-joint fluid was aspirated and hydrocortisone was injected intra-articularly every two to four weeks. Later it was necessary to aspirate 50 to 100 cc. of fluid and inject 50 mg. of hydrocortisone in each knee every one to two weeks for six or seven months. Synovectomy was recommended but the patient refused. Hydrocortisone, 60 mg. daily orally, was successfully tried but a gastric reaction occurred. When the dosage was reduced to 30 mg. daily, bilateral knee-joint effusion recurred. The erythrocyte sedimentation rate ranged from 55 to 20 mm. over a period of eight years. Meticorten was started November 29, 1954, when the sedimentation rate was 28 mm. per hour (Westergren corrected). Five days after initiation of this treatment (on 30 mg. a day) the patient showed remarkable improvement and was able to flex the fingers nimbly. The dose was reduced to 20 mg. Eight days after starting this therapy, there was much less swelling of the knees and the patient said he hadn't used his hands with such ease in ten years. The sedimentation rate had dropped to 6 mm. On the twenty-fourth day the dose was reduced

to 17.5 mg. and on the thirty-first day, to 15 mg. The hands could be made into fists, and there were no swellings. The knees were objectively normal. The limitations of movement in the elbow and shoulder had cleared. On the fifty-first day, the ankylosis (fibrous) of the wrists had decreased to 10 per cent, from an original level of 50 per cent. On the seventieth day, the wrists were normal. One hundred and six days after starting treatment the reversal was being maintained. The total dose of Meticorten had been 1,630 mg.

In the foregoing case reports, rehabilitation of the knees as well as the hands was demonstrated. Although corrective procedures are usually more successful when dealing with knee joints than with finger joints, many attempts at straightening knees were unsuccessful. From this point of view the following case would appear to be worth mentioning.

Case 3. This patient, a female aged 60, had been treated by an orthopedic surgeon two years before for badly flexed knees. They were partially corrected by wedged casts and intra-articular hydrocortisone. The joints had remained painfully limited in motion, were swollen, tender, and showed flexion contractions of 25° and 10°, respectively. After one month on Meticorten therapy, swelling, pain and stiffness disappeared. One knee could be completely extended and the other was within 10° of normal. This case, in which faulty postural alignment and continued inflammation were great handicaps, was definitely relieved by treatment with Meticorten.

The following case presents the problem of the prevention of ulnar deviation.

Case 4. The patient, a woman 44 years of age, had had rheumatoid arthritis for fifteen years. She had formerly received cortisone, hydrocortisone, ACTH and 15 metacarpophalangeal injections in an attempt to prevent ulnar deviation. The sedimentation rate had fallen from 28 to 13 mm. per hour. The periarticular swellings were partially reduced. Meticorten was started in a dosage of 20 mg. daily. Within twenty days the swellings disappeared and a maintenance dose of 15 mg. was successfully continued. The total amount of Meticorten administered was 840 mg.

We have learned that when the "splinting" inflammation is rapidly absorbed around joints, there is danger of increased subluxation unless the joints are supported until atrophic muscles can be strengthened.

Among the 44 rheumatoid arthritis cases, in only 1 instance was Meticorten therapy a complete failure, as outlined in the following abstract:

Case 5. The patient was a woman 33 years of age, suffering from active generalized rheumatoid arthritis. The dosage of Meticorten ranged from 20 to 30 to 40 mg. daily, totalling 2,110 mg., without the slightest subjective or objective response. We had formerly treated this patient successfully with supportive measures, gold salts, and cortisone during her initial illness. After the disease had apparently been arrested, she had gone to Minneapolis in the summer of 1954, for three months and was well without treatment. Soon after returning in October 1954, there was a severe recurrence in all joints. The attack was worse than the initial one, and was clinically typical of rheumatoid arthritis. Focal infection, gout and brucellosis were carefully ruled out. The patient is now hospitalized for further metabolic and endocrine studies.

It is understood that complete remission of rheumatoid arthritis includes reversal of the erythrocyte sedimentation rate. Elevated sedimentation rates became normal in most cases within a week; none required more than two weeks, with 1 exception, in which the time required was one month.

The patients reported a feeling of well-being and increased initiative twenty-four hours after Meticorten was started. The rate of improvement in the joints followed a certain pattern. Pain and stiffness were first relieved over a period

ranging from one to seven days; reduction of swelling and tenderness followed. In the early cases, swelling and tenderness disappeared within a week; in the chronic ones, this process took from two to four weeks. In 1 case, complete reversal required seventy days. Obviously, in some of the patients who started later in the series, the improvement may ultimately be grade I instead of grade II.

So far, maintenance doses of Meticorten have been much more effective than safe doses of cortisone. If the potency of Meticorten is 3 to 5 times that of cortisone, such a difference should be considered. It is too early to know how lasting its beneficial effects may be and to know whether or not its prolonged use may ultimately produce "Meticorten fastness." In the case of cortisone, we know that with continuous use it finally becomes ineffective even in large doses, and its withdrawal becomes difficult.

Although we consider Meticorten far superior to cortisone and other steroids in the treatment of rheumatoid arthritis, its use should not preclude 1) the necessity for employing tried and true supportive measures such as rest, adequate diet, physical therapy, and corrective orthopedic measures when indicated; 2) the control of focal infection; 3) attention to allergic, occupational and social environmental factors; and 4) other conditions pertaining to the general health of the patient.

The rationale of a potent anti-inflammatory agent in rheumatoid arthritis becomes clear through the study of microscopic sections from the swollen synovia and periarticular thickening. The dense cellular infiltration of fibroblastic tissue apparently is absorbed more completely during Meticorten therapy than during treatment with any analogous product heretofore introduced.

RHEUMATOID SPONDYLITIS

In the 3 cases of rheumatoid spondylitis, pain was relieved. Postural improvement was noted in the 2 patients with fibrous ankylosis; there was no improvement in the 1 with bony ankylosis.

DERMATOMYOSITIS

Management of the case of dermatomyositis was difficult. Cortisone had proved to be over-stimulating, causing extreme euphoria verging on a mental complication. Meticorten relieved pain and cleared a persistent skin rash but had little effect on the profound weakness. Reaction alternated between mild elation and deep depression. Slight hirsutism developed the third week. The total dose of Meticorten was 1,350 mg.

GOUTY ARTHRITIS

In 1 moderately advanced case in a female patient, aged 54, there was prompt, complete remission of a subacute persistent attack in the metatarsophalangeal joints. Both joints had been swollen, red and sensitive. Former attacks had responded to colchicine. The blood uric acid level was 6.8 mg. per 100 ml. Only time will tell whether or not maintenance dosage of Meticorten will prevent further gouty attacks. In 2 advanced cases of gouty arthritis, the course was as follows:

Case 1. One patient with extensive soft tissue tophaceous deposits "got more relief from this new medicine than from anything else; wore shoes I couldn't wear for four years."

Case 2. The other patient was a young man. The history and early course, including early wrist ankylosis, were typical of rheumatoid arthritis and he was given appropriate treatment. A large fluctuating swelling around the shoulder joint finally cleared up during Butazolidin therapy; a "wrist ganglion" yielded uric acid crystals. X-ray examination of the joints showed extensive destructive changes characteristic of gouty arthritis. One determination of the blood uric acid level showed an elevation to 6.9 mg. per 100 ml.; twelve others showed normal levels over a period of five to six years. The patient was greatly relieved by Meticorten. After two weeks of treatment, he could stand for five or six hours—something he had not been able to do for two years. Benefit will be limited to absorption of secondary inflammatory products around the irreversible destructive changes.

OSTEOARTHRITIS

Four cases are reported; 2 involved the knees and 2, the spine.

In 1 instance both knees were enlarged with general, not trigger-point, tenderness. By x-ray examination they showed marked hypertrophic changes, and were very painful on walking. This patient came from a distance for the temporary relief she obtained from intra-articular hydrocortisone injections. In December 1954, injections of hydrocortisone were given and also sufficient Meticorten tablets to be taken twice daily for a month. At the end of that time the patient wired for more tablets and in February when she returned she was more interested in receiving Meticorten than in receiving injections. In this case we may assume that there were inflammatory deposits around the extensive bony overgrowths.

The second case was that of a woman, 77 years of age, whose left knee was chiefly affected. There was tenderness over the mesial meniscus, marked synovial swelling, swelling of the popliteal bursa, and x-ray evidence of osteoarthritic changes. The response to Meticorten was prompt and complete.

In the cases involving the spine, presumably bony spurs and secondary inflammatory swelling impinged upon nerve roots at their exits through the foramina. Meticorten relieved pain in both cases—in one, after a decompression operation.

INTRACTABLE TORTICOLLIS

This patient presented marked lateral deformity, which had been present for fifteen years. There was moderate improvement following cortisone and physical therapy, at which time an orthopedic consultant stated that nothing more could be done in such a chronic case with ankylosis and extensive bony hypertrophic changes. To our amazement "something gave way" after seven days of Meticorten therapy. The head was held erect and it could be moved in all directions with very little resistance and without pain.

REFRACTORY BURSITIS

This case was an enigma. How could a condition which had been present for months and required strong opiates, be so promptly, completely and lastingly relieved? Cortisone and Novocain plus hydrocortisone injections had been entirely ineffective. Butazolidin had also been tried unsuccessfully. The patient was unable to work and could not sleep. There was definite relief after he took 4 or 5 Meticorten tablets and he came in almost "dancing." Complete relief was obtained in ten days, enabling the patient to return to work. This status had not changed at a check-up two months later.

SIDE EFFECTS

Undesirable reactions do occur with Meticorten, but they are less frequent, less severe, less varied and more transitory than with cortisone. Reactions, such as mild insomnia and nervousness and digestive disturbances, tend to decrease and disappear in many cases as the drug is reduced or, in certain cases, even when the dose is not altered. Increased appetite, insomnia, gastric disturbances, mild euphoria, facial rounding, palpitation, weakness, perspiration, hirsutism and depression have occurred in that order. With Meticorten, body weight tends to be steady or to show a slight decrease, in contradistinction to cortisone, with which the average gain in our group of 228 cases studied in 1951 was 15 pounds. There is in our experience no impairment of water balance during Meticorten medication. Urination is increased early, during the first seven to ten days, in both frequency and volume. Blood pressure readings remain unchanged, the blood sugar level remains normal and blood counts are unaffected.

Of the reactions encountered, cardiac episodes were most troublesome and usually took the form of heart consciousness, palpitation, breathlessness and precordial oppression. There were no cases of cardiac decompensation. Only 1 cardiac reaction in our group was severe enough to stop treatment. Gastric reactions deserve attention, especially with history of unusual indigestion. The steroid was temporarily discontinued in 3 such cases.

COMMENTS

Meticorten is therapeutically more potent and, to date, its use is attended by less clinical toxicity than any of its steroid predecessors. Roughly speaking, we may say it is four times more potent than cortisone and one quarter as toxic. At a comparable period in clinical research with cortisone, the results were not as good as with Meticorten and there was far less assurance of safety. When Meticorten is discontinued symptoms and signs recur within about the same period of time as following the withdrawal of cortisone.

CONCLUSION

Meticorten is more effective in the treatment of inflammatory arthritic and allied conditions than cortisone and its analogues. The response is more rapid, the effect is more prolonged between doses, and maintenance is better with small doses. Meticorten is a more potent anti-inflammatory agent; there is, therefore, complete reversal of residual as well as active periarticular swellings. Side effects are comparatively infrequent and minor.

This is a preliminary clinical study and further observations are required in order to determine the ultimate effect of prolonged administration of this steroid.

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Abstracts of Current Literature

TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS.
Bunn, P. A., and Cook, E. T. *Ann. Int. Med.* **41:** 487 (Sept.) 1954.

The treatment of subacute bacterial endocarditis is reviewed. Of 48 patients with this infection, 15 died. Causative micro-organisms were not recovered during life from 10 patients. Organisms resistant to more than 1.5 units of penicillin per milliliter were present in 11 patients; in 1 the organism became insensitive to all antibacterial agents. Forty-seven patients received penicillin, 16 streptomycin in addition, and 4 other adjuvant antimicrobial agents. One received streptomycin, oxytetracycline, chloramphenicol, chlortetracycline hydrochloride, and sulfonamides. The dosage of penicillin or streptomycin was based on the measured sensitivity of the causative organism. Excessive amounts of both had to be used when there was a high level of resistance to penicillin. Antimicrobial therapy was continued three weeks after the cessation of evidence of active infection. Accessory therapy was prescribed as indicated. Two thirds or more of patients should recover under a wisely designed and managed program such as this. Reasons for unsuccessful management include resistant organisms, insufficient antimicrobial therapy, or irreversible heart failure. Perforation or rupture of the aortic valve caused death in 6 of the 15 patients in the reported series. No preventive measures are suggested. Early diagnosis and institution of therapy are essential. Antimicrobial agents are limited in usefulness to eradication of the organisms that stimulate pathologic changes. The prognosis in patients cured of subacute bacterial endocarditis is good for long-term health, except in those with aortic insufficiency or heart failure. A patient can, however, become reinfected.

TACE IN PROSTATIC CANCER: CLINICAL AND BIOCHEMICAL CONSIDERATIONS.
Carroll, G., and Brennan, R. V. *J. Urol.* **72:** 497 (Sept.) 1954.

A series of 42 patients suffering from prostatic cancer has been treated by surgical methods and the new synthetic estrogen, TACE, during a period of thirty-two months. TACE was well tolerated even when extremely large doses were administered and there was a virtual absence of undesirable side effects. In many patients in whom the disease had become resistant to other synthetic and natural estrogens the administration of TACE resulted in clinical improvement. This was characterized by an increase in weight, a decrease in pain, an improvement in the blood picture, and regression of metastatic lesions. In 5 TACE-treated patients who came to autopsy there was no evidence of the adrenal hyperplasia which has been observed in laboratory animals following the administration of some other synthetic estrogens. Sufficient time has not elapsed to compare the survival time in TACE-treated patients to that observed in patients treated with other synthetic or natural estrogens. The urinary excretion of 17-ketosteroids was investigated in 21 patients who had received daily doses of 24 to 180 mg. of TACE for many months and the findings indicate that the administration of TACE has no adverse effect upon adrenocortical function. The significance of determination of 17-ketosteroids in prostatic cancer is discussed. (Authors' summary and conclusions.)

MANAGEMENT OF HYPERTENSIVE DISEASE.
Corcoran, A. C.; Dustan, H. P.; Taylor, R. D., and Page, I. H. *Am. J. Med.* **17:** 333 (Sept.) 1954.

The pharmacotherapy and management of severe hypertensive disease are reviewed primarily with regard to hydralazine and hexamethonium. The former gives sustained relief and decreases mortality in about half of the patients treated; its use is complicated by

common, usually transitory side effects and, in some patients, by a delayed toxic response characterized as a rheumatic and febrile syndrome. Experience with the use of hexamethonium alone shows that it gave temporary relief in 16 of 17 patients with malignant hypertension; the duration of relief was limited by tolerance to its depressor effect on supine diastolic pressure. Benefit was not determined by persistence of orthostatic hypotension. Some additive effects of combined treatment with hexamethonium and hydralazine were defined in 7 of 14 patients tested with these drugs separately and in combination. However, only 2 gained more than 10 mm. Hg decrease in average supine diastolic pressure from the combination. Side effects of hydralazine were not mitigated by effective doses of hexamethonium. Preliminary observations indicate that reserpine (Serpasil) is a potent antipressor in some patients when used alone or in association with other drugs. In perspective, the considerable efficacy of specific agents and procedures in some patients, but not in others, suggests that hypertension in these is sustained by different, definable mechanisms. Insight into these should diminish the large measure of poorly rationalized empiricism which presently clouds the treatment of hypertensive disease. (Authors' summary.)

RECENT ADVANCES IN NUTRITION AND METABOLISM. I. REVIEW OF THE LITERATURE ON GENERAL NUTRITION AND PROTEIN AND MINERAL METABOLISM, 1952.
Davidson, C. S. *A. M. A. Arch. Int. Med.* **94:** 460 (Sept.) 1954.

This article cites recent nutritional investigations. The medical aspects of nutrition are reviewed as related to: 1) measurement of body composition, 2) nutrition, aging, and chronic disease, 3) liver disease, 4) obesity, 5) protein and amino acids, 6) sodium and potassium, 7) fluorine, 8) iron, 9) copper, 10) cobalt, and 11) zinc.

STUDIES OF APPETITE AND OF CONSTIPATION IN ADVANCED LIFE: PSYCHOLOGICAL AND STATISTICAL EVALUATION OF A COUNTY HOME SURVEY IN IOWA.
Ginzberg, R., and Brinegar, W. C. *Am. J. Digest Dis.* **21:** 267 (Sept.) 1954.

One hundred and twenty-six elderly county home residents in the northwestern part of Iowa were interviewed. The data obtained were verified as far as possible by comparison with other data. The mean age of the group was 75.2, the oldest subject being 96 and the youngest 65 years of age. Appetite was found to be good or fair in 82 per cent of the subjects. Constipation was found in 17.4 per cent of all subjects and in 24.3 per cent of the nonpsychotic and mildly mentally ill. In the latter group, however, only 17.1 per cent had less than one bowel movement per day, and only 12.9 per cent had to take laxatives. It was possible to make a statistical evaluation of the data, particularly those concerning constipation, since questions regarding digestive functions were included in the survey questionnaire, which was primarily directed toward investigating social and psychologic aspects of elderly residents of county homes. It was found that correlations between constipation, insomnia, and length of stay in the county home were of statistical significance. An analysis of these findings is given. This study casts doubt on the widespread belief that poor appetite and constipation are major problems among elderly individuals. Further study is therefore advocated.

THE RELATIONSHIP BETWEEN THE THIRD VENTRICLE AND THE BASILAR ARTERY.
Greitz, T., and Löfstedt, S. *Acta radiol.* **42:** 85 (Aug.) 1954.

The relation between the floor of the third ventricle and the basilar artery has been studied both roentgenologically and at autopsy. Five cases with a basilar impression in the floor of the ventricle are described. From clinical, roentgenologic, and pathologic-anatomic observations the authors have found that the deformation of the third ventricle caused by the basilar artery only occurs when the latter is enlarged. It is considered likely that this enlargement is principally caused by damage to the elastic tissue in the vessel, combined with high blood pressure. (Authors' summary.)

SUBACUTE COMBINED DEGENERATION OF THE CORD AND ACHLORHYDRIC PERIPHERAL NEUROPATHIES WITHOUT ANAEMIA.

Jewesbury, E. C. O. *Lancet* **2:** 307 (Aug. 14) 1954.

Subacute combined degeneration of the cord may be associated not only with a normal peripheral blood count but also with a normal sternal marrow. Five cases are described with insignificant changes in the peripheral blood and with normoblastic bone marrow. Changes characteristic of pernicious anemia were found in the peripheral blood and bone marrow after one year in a patient who initially received no vitamin B_{12}, and after three years in another who received only a small amount. In 3 patients adequately treated, pernicious anemia did not develop (in 2, metamyelocytes were seen in the bone marrow), neurologic signs did not advance, and symptoms regressed. In 2 patients peripheral neuropathy was associated with histamine-fast achlorhydria and a normal peripheral blood count. In one of them minimal changes in the sternal marrow suggested the beginning of pernicious anemia. Patients with histamine-fast achlorhydria are in varying degrees likely to show signs of vitamin B_{12} deficiency (peripheral neuropathy, subacute combined degeneration, pernicious anemia), but the relative susceptibility of the peripheral nerves, spinal cord, and bone marrow is unpredictable. Early treatment of neurologic manifestations is essential, and such patients should be kept under prolonged observation. Although always suspect, some cases of peripheral neuropathy with histamine-fast achlorhydria and without anemia are due to causes other than vitamin B_{12} deficiency. The inappropriate terms "pernicious anemia" and "subacute combined degeneration of the cord" should be dropped in favor of the designation "vitamin B_{12} deficiency," qualified, if desired, by adding "megaloblastic anemia" or "neuropathy."

CARCINOMA OF THE PARANASAL SINUSES AND THE NASAL CAVITIES.

Larsson, L-G., and Mårtensson, G. *Acta radiol.* **42:** 149 (Aug.) 1954.

An evaluation is made of results of treatment during the period 1940–1950 of 344 cases of carcinoma arising from the mucous membranes of the paranasal sinuses and the nasal cavities. More than two thirds of the 379 patients referred (45 were not admitted for treatment because of advanced age, tumor extension, or poor condition) were aged 50 to 70 years and equally divided as to men and women. These carcinomas tend to arise from mucosal changes associated with chronic inflammatory processes. The most frequent early symptoms (pains, nasal secretion, obstruction) resemble those of sinusitis. Bulging of the face or oral cavity, dislocation of the eye, and bleeding from tumor masses in the nasal cavity are late signs indicating penetration of bony walls. Sanguinous nasal secretion is an important sign but may not occur early. Early symptoms are in general nonspecific and negative findings on roentgen examination do not exclude a malignant tumor. Chronic sinusitis should not be treated conservatively over a long period and any tissue removed at minor operations should be examined histologically. The first step in treatment is to determine operability. Absolute contraindications to surgery are destruction of the base of the skull or pterygoid process, tumorous infiltration of the mucous membrane in the nasopharynx, inoperable lymph node metastases, and generalized metastases. The technic developed during the 10-year experience is preoperative roentgen irradiation with from 2,000 to 2,500 r for each of four facial fields, with radical operation in four to six weeks and insertion of radium tubes into the operation cavity. Inoperable and borderline patients receive roentgen irradiation with 3,000 r per field, by which some may be rendered operable. The operative procedure consists of destruction of the tumor and adjacent tissues by electrocoagulation and removal of these parts by forceps. Chemotherapeutic agents and antibiotics are given both pre- and postoperatively. The following five-year cure rates were obtained (years 1940–47): overall, 27 per cent; among surgically treated patients (electrocoagulation combined with radiotherapy), 45 per cent; among patients treated radiologically (largely inoperable), 12 per cent. Of the patients who were operated on, 13 (11 per cent) died, 6 of them of cerebral

complications. Changes due to radiotherapy included minor cutaneous lesions, pronounced atrophy of the nasal mucous membrane, crust formation, atrophic rhinitis, cataract, and skeletal changes with decalcification. Healing was not delayed if the operation was performed within one or two months after irradiation. The tumor recurred in 27 per cent of the surgical patients. Of 12 reoperated on, 1 was alive and well after five years and 1 after three years; the tumor could not be eradicated in the other 10. Among the 334 tumors, there were 156 well differentiated squamous-cell carcinomas, 60 poorly differentiated squamous-cell carcinomas, 34 cylindric-cell carcinomas, 52 unspecified, 11 adenocarcinomas, and 21 not diagnosed pathologically. Poorly differentiated or undifferentiated carcinomas showed the highest incidence of metastases and poorest prognosis, whereas cylindric-cell carcinomas showed the opposite.

THE SURGICAL TREATMENT OF WRINKLES.

Lewis, G. K. *A. M. A. Arch. Otolaryng.* **60:** 334 (Sept.) 1954.

Various causes of wrinkles and sagging skin of the face, forehead, glabellar region and eyelids are discussed, with the essential reasons for their surgical correction. A successful technique of operation employed for removal of wrinkles and redundant skin is described. The good results obtained and the prognosis of long-lasting corrections are attributed in large measure to location of the operative incision. Importance of rhytidoplasty is stressed for enhancement of the industrial, sociologic, and psychologic rehabilitation of the growing senescent population and for the correction of wrinkles and sagging skin resulting from disease. (Author's summary.)

POSSIBILITA DI TRATTAMENTO CHIRURGICO ASSOCIATO AD ORMONO TERAPIE IN FRATTURE PATOLOGICHE DA METASTASI TUMORALI (POSSIBILITY OF SURGICAL TREATMENT ASSOCIATED WITH HORMONE THERAPY IN PATHOLOGICAL FRACTURES CAUSED BY METASTASES FROM TUMORS).

Zappala, G. *Policlinico* **61:** 347 (March 15) 1954; through Pfizer Hormone News Letter, September 1954.

Two patients with fractures following operations for breast epithelioma are reported. Both underwent operation for the fracture and received 25 to 50 mg. of testosterone propionate daily. After eight months they could walk in almost normal fashion. Androgen therapy permitted treatment of these pathologic fractures in the same manner as nonpathologic fractures.

CORTISONE TREATMENT IN ADVANCED CARCINOMA OF THE PROSTATE.

Miller, G. M., and Hinman, F., Jr. *J. Urol.* **72:** 485 (Sept.) 1954.

Ten patients with disseminated carcinoma of the prostate in a state of severe exacerbation following previous remission from orchiectomy and estrogen therapy were treated with cortisone, starting with 50 mg. per day by mouth in divided doses. Eight of the 10 patients had marked subjective improvement and 6 of the 10 had objective improvement, with decrease in the size of the local lesion. In 2 there was a decrease in the level of acid phosphatase. These results are comparable to those reported after bilateral adrenalectomy. The duration of beneficial response (eighty-two days, on the average) was probably shorter than after surgical adrenalectomy. Hormonal studies were made and their contribution to our knowledge of hormonal interrelationships in carcinoma of the prostate is discussed.

MALIGNANT DEGENERATION IN ATROPHY OF THE STOMACH AND PERNICIOUS ANEMIA.

Niemetz, D., and Mead, F. B. *Am. J. Gastroenterol.* **22:** 217 (Sept.) 1954.

One hundred and ten patients with atrophic gastric mucosa, ranging in age from 18 to 93 years, were examined in order to determine the incidence of carcinoma of the stomach

associated with this change. Eighty-five of the group had pernicious anemia, diagnosed by standard methods. The diagnosis of atrophy of the gastric mucosa was established by gastroscopy or microscopic examination of autopsy material. No malignant gastric disease was found among the 25 patients with gastric mucosal atrophy alone. In the pernicious anemia group, 3 patients (3.5 per cent) had malignant neoplasms of the stomach, but none of these was proved to be carcinoma. This agrees well with the reported incidence of 3 to 10 per cent for gastric carcinoma developing in patients with pernicious anemia.

SPINAL DECOMPRESSION IN POTT'S PARAPLEGIA.

Nisbet, N. W. *Lancet* **2:** 303 (Aug. 14) 1954.

Pott's paraplegia sometimes disappears spontaneously. However, because of the great danger of permanent spinal cord injury, spinal decompression should not be delayed. Patients must be carefully selected, because a high mortality rate accompanies the operation. Radiologic examination offers little in deciding when to operate or the type of operation to use. Anterolateral rachitomy meets the requirement that in the procedure decompression be extensive enough to relieve the compression, but the operation not so extensive as to jeopardize the stability of the spine. In most cases requiring operation, mechanical compression of the theca interrupts spinal conduction. Edema, pachymeningitis, myelitis, and vascular thrombosis are probably unusual indirect causes, inasmuch as rapid recovery often follows spinal decompression.

TREATMENT OF PROSTATIC CARCINOMA WITH RADIOACTIVE COLLOIDAL CHROMIC PHOSPHATE (P^{32}): A PRELIMINARY REPORT.

Rusche, C., and Jaffe, H. L. *J. Urol.* **72:** 466 (Sept.) 1954.

Twenty-eight prostatic carcinomas were treated with colloidal radioactive chromic phosphate. Among its advantages over radioactive gold are its emission of beta rays alone and a longer half-life. The patients ranged in age from 54 to 81 years. All were in the second stage of the disease with bladder-neck obstruction in 8, acute retention in 13, and unilateral or bilateral extension to the seminal vesicles in all. As the smaller the prostate the better the response, large amounts of prostatic tissue were removed transvesically before injecting the radioactive phosphorus into several sites transvesically. A dose of from 0.3 to 0.5 millicurie per gram of involved tissue was injected, the total dose varying from 6 to 40 mc. The prostates decreased in size in 18 patients, softened in 4 and became firmer in 14. In 14 the decrease in size was remarkable and the change in consistency occurred within thirty to sixty days following treatment. Biopsy specimens were taken at three months in 10 of the patients and at twelve months in 1. All showed some active tumor cells, indicating that the process was not destroyed in any case, although diffuse fibrosis and necrosis had taken place in some areas. No serious complications occurred. Mild bladder discomfort subsided in thirty to forty days. A small amount of the radioactive material entered the blood stream but produced no late changes in blood or bone marrow. The liver was the only body organ in which radioactivity could be demonstrated.

RESULTS OBTAINED BY ENDOCRINE CONTROL THERAPY FOLLOWED BY RADICAL PERINEAL PROSTATECTOMY IN TWENTY-FIVE SELECTED CASES OF ADVANCED CARCINOMA OF PROSTATE.

Scott, W. W. *J. Urol.* **72:** 504 (Sept.) 1954.

The patients considered are those with advanced carcinoma of the prostate without metastasis, in whom the carcinomatous extension beyond the confines of the prostate although not marked, is too great to permit complete extirpation by radical operation at the time the patient is examined. If the response to estrogen therapy is such that digital examination at the time of maximum regression suggests that complete extirpation may be possible, then a radical perineal prostatectomy may offer a chance of cure or prolong the patient's life and his freedom from distressing symptoms. Some patients must be excluded because of ad-

vanced age or poor physical condition. The survival rate for thirty-six months in a series of 25 patients treated in this manner was 84 per cent, compared with the reported rates of 20 per cent in a control series, 49.7 per cent in stilbestrol-treated patients, 53.4 per cent in castrated patients, and 66 per cent among patients castrated and treated with stilbestrol. These results warrant further trial of the therapy. The operation entails little, or no more risk than other open operations for prostatic obstruction. Estrogen therapy postoperatively should be prolonged.

SUBJECTIVE MANIFESTATIONS OF ACUTE CORONARY OCCLUSION OR INSUFFICIENCY. THEIR RELATION TO AREA OF RESULTING MYOCARDIAL INJURY.

Sigler, L. H. *A. M. A. Arch. Int. Med.* **94:** 341 (Sept.) 1954.

Early subjective manifestations of acute coronary occlusion and of coronary insufficiency were studied in 1,200 patients. Among them, 974 had a subsequent course of myocardial infarction and 226 of myocardial ischemia or ischemic necrosis. The characteristic constricting pain was the most common complaint; but in 4.4 per cent there was no pain, and in 15.6 per cent pain did not aid in the diagnosis. In other patients it was not of the usual type. In order of frequency, pain radiated to the following areas: upper extremities and back of the chest, epigastrium and abdomen, head and neck. It often radiated to more than one area. The sensation in the area of radiation many times differed from that in the area of origin. Some pain originated outside and radiated to the anterior chest. Pain occurred relatively more frequently in the entire anterior chest or in the retrosternal region and tended to radiate relatively more often to the head and back in left ventricular anterior-wall infarction than in posterior-wall infarction. In posterior-wall infarction, pain was more frequent in the precordial region and radiated more often to the neck, upper extremities, or epigastrium. It was more often absent here than in anterior-wall infarction. Other complaints besides pain were (in percentages of patients): sweating, 62.9; weakness, 18.2; other constitutional symptoms, 7.2; cerebral symptoms, 21.6; gastrointestinal symptoms, 15.8; respiratory symptoms, 11.3; complaints referable to the heart, other than pain (palpitation, "pounding," "thumping") 2.4. Cerebral, gastrointestinal and respiratory disturbances were more common in posterior-wall infarction. The early subjective manifestations of coronary insufficiency resemble those of coronary occlusion but the pain usually is milder and more intermittent. Pain occurs more frequently in the retrosternal region and radiates less frequently to the epigastrium. Weakness and cerebral and gastrointestinal disturbances are less frequent. The physiologic mechanism of the subjective manifestations is discussed. The heart is considered to have extensive sensory receptors, with emerging afferent nerve fibers making widespread synaptic connections with efferent neurons in the vegetative nuclei of the hypothalmic region. The variations in symptomatic expression of an acute cardiac insult appear to be due to differences in the location and extent of sensory receptors in the heart and of synaptic connections in the central nervous system, as well as to individual differences in the interpretative ability of the higher centers. (Excerpt of author's summary.)

THE PRODROMAL SYMPTOMS OF MYOCARDIAL INFARCTION.

Smith, H. J., and Buchman, D. M. *J. Iowa State M. Soc.* **44:** 412 (Sept.) 1954.

The clinical histories of 100 consecutive cases of myocardial infarction were studied for evidence of prodromal symptoms. In 48 patients warning symptoms were noted from three months to one day before the clinical picture of infarction appeared. In only 2 did these symptoms appear more than six weeks before the attack. In order of decreasing frequency, the symptoms were: sudden onset of anginal pain, unusual dyspnea, and an abrupt change in the character of a previously existing angina pectoris. The pathology of coronary arterial occlusion is briefly reviewed. If any clinical advantage is to be gained by early recognition of impending myocardial infarction, measures must be available to forestall critical dimi-

nution of the blood and oxygen supply to the heart muscle. Reduction of cardiac work is the most obvious approach and there is some evidence that rest may decrease the severity of symptoms, although not prevent infarction. The use of anticoagulants in an attempt to forestall thrombosis entails an increase in the risk of hemorrhage into the wall of the coronary artery. The use of large doses of vitamin K parenterally, to safeguard against intramural coronary hemorrhage, may invite thrombus formation within the narrowed lumen. Until better clinical criteria are available for differentiating intramural hemorrhage and coronary-vessel thrombosis, anticoagulant therapy will be largely empirical. Attention to the clinical history may yield a higher percentage of cases of myocardial infarction in which warning symptoms can be elicited.

LUMBAR HERNIAS.

Swartz, W. T. *J. Kentucky M. A.* **52:** 673 (Sept.) 1954.

Two cases of lumbar hernia are presented. Both had origin through the superior lumbar triangle. Although these lesions may be congenital, occurring usually bilaterally, the majority of cases are acquired. These may be spontaneous (congenital weakness plus an indirect injury), or traumatic (secondary to surgery, severe trauma or infection). Thorek classifies them according to their peritoneal component, extra-saccular, para-saccular or intra-saccular. Sac contents vary but usually consist of properitoneal fat or bowel. Symptoms vary from vague aches to severe colicky pains. Strangulation occurs in about 10 per cent of the reported cases. The cardinal diagnostic triad includes a palpable, reducible, flank mass which transmits an impulse. Fundamentals of repair and various procedures are described. The author has used a type of repair in which fascial strips are taken from the thigh. With these, the transversalis fascia is imbricated and the adjacent musculo-fascial walls approximated. This repair is reinforced by additional fascia woven between the previous loops and forming a solid, living, fascial support to the triangle. (Author's summary.)

ENDOCRINE INHIBITION AS RELATED TO CARCINOMA OF THE PROSTATE.

Valk, W. L., and Owens, R. H. *J. Urol.* **72:** 516 (Sept.) 1954.

Far-advanced relapsing carcinoma of the prostate in 12 patients was treated with a combination of cortisone and stilbestrol. An initially high cortisone dosage was used in an attempt to inhibit the adrenal and anterior pituitary glands and thus suppress the elaboration of androgen. Stilbestrol served as an adjunct to pituitary inhibition. The regimen was as follows: bilateral orchiectomy; 5 mg. of stilbestrol daily for life; cortisone, 300 mg. per day for two weeks, followed by 200 mg. per day for two weeks, then 100 mg. per day for two weeks, and then 25 mg. per day for life; low-salt diet; 2 to 3 Gm. of potassium chloride daily; an antacid regimen if there was a history of peptic ulcer; and diuretics as needed. Five patients are living and 3 of them are asymptomatic. The duration of treatment in the 5 was from six to nineteen months. Seven patients died from progressive carcinomatosis or complications of therapy. Two patients expired when they inadvertently discontinued cortisone for one or two weeks. One showed signs of adrenal insufficiency. Urinary 17-ketosteroids were markedly depressed in 7 patients, indicating adrenocortical inhibition. This small series indicates that approximately 40 per cent of patients with far-advanced prostatic carcinoma can obtain additional benefits from therapy with cortisone and stilbestrol in combination. The use of this combination is suggested in patients who have become refractory following previous orchiectomy and stilbestrol therapy.

HIGH BLOOD PRESSURE IN OLDER WOMEN.

Wakefield, H. *Postgrad. Med.* **16:** 175 (Sept.) 1954.

A study at an Old People's Home of the 20-year records of some 500 women between the ages of 70 and 100 years showed essential hypertension in about 75 per cent. The pattern of the elevated blood pressure was similar in the decades beyond the age of 70 years. No per-

manent remission was seen after essential hypertension had been diagnosed; neither did uremia, renal failure or severe nitrogen retention occur. The eyegrounds in most patients showed only benign lesions, some low-grade arteriosclerosis, few hemorrhages or exudates, and no papilledema. Elevated blood pressure in many of the 500 women had its onset between the ages of 30 and 45 years. Few older women have symptoms referable to the blood pressure level. The blood pressure level apparently does not affect the rate of progression of other disorders, or the subsequent development of complications. The chief cause of death is congestive heart failure. Coronary artery disease and cerebral vascular accidents are less frequent. When acute coronary thrombosis occurs, the mortality is high. These older women are more likely to die from neoplastic disease than from complications of hypertension. The only treatment used in the 20-year period was encouragement, reassurance and optimism. As the pathogenetic mechanism of essential hypertension is unknown, the author believes there is no specific therapy.

THE AMERICAN MEDICAL WRITERS' ASSOCIATION

The 1955 meeting of the American Medical Writers' Association will be held in the Jefferson Hotel, St. Louis, Missouri, September 30–October 1. A special feature of the meeting this year will be the second half-day program (Saturday morning, Oct. 1) comprising a four-hour Workshop on Medical Writing to be conducted by faculty members from the Schools of Journalism of the Universities of Illinois, Missouri and Oklahoma. These universities are conducting four-year courses in medical journalism and medical writing, initiated and approved by this Association. Association members may attend this Workshop without charge; a $5.00 registration fee will be charged non-members.

In the January 1955 issue of the Mississippi Valley Medical Journal there is interesting information concerning the American Medical Writers' Association. The issue is devoted to papers read at the 1954 meeting in Chicago. These papers are available in a reprint entitled "1954 Symposia on Medical Writing" and may be secured for 25 cents postpaid from the Headquarters of the Association, 209–224 W. C. U. Building, Quincy, Illinois.

Harold Swanberg, M.D.
Secretary

THE HEBREW MEDICAL JOURNAL COMMEMORATES THE 750TH ANNIVERSARY OF MAIMONIDES' DEATH

The Hebrew Medical Journal, under the editorship of Moses Einhorn, M.D. of New York, has marked its twenty-seventh year of existence by the issue of two volumes in 1954. Written in Hebrew, with English summaries, the journal has played an important part in the creation of a medical literature and terminology in the language of the Bible.

Volume 1, 1954, includes, besides the medical articles, a comprehensive study by Dr. Z. G. Raphaely of local problems of psychiatric treatment in Israel. In the section on "Historical Medicine," Dr. L. M. Herbert describes the life and work of the physician, Rabbi Jacob Zahalon, a remarkable personality in the world of Hebrew letters and Hebrew medical writings of the seventeenth century. His medical encyclopedia "The Treasure of Life," published in 1683, is truly an epitome of the medical knowledge of his day.

The section on "Old Hebrew Medical Manuscripts" contains an enlightening treatise on the "Book of Medical Experiences," ascribed to Rabbi Abraham Ibn Ezra (11th century), by J. Leibovitz, M.D. of Jerusalem. The systematic arrangement of the book into diseases and symptoms gives us a broad picture of the medical problems with which the author was faced, as well as an idea about medieval pathology in general. The section on "Talmud and Medicine" contains a very interesting article by Dr. Benjamin L. Gordon on "Medicine Among the Ancient Hebrews."

Volume 2, 1954 includes an exhaustive study on "Gerontology with Special Reference to Israel" by Dr. Ch. Nitzany. The author points out that although in Israel the problem of gerontology seems to be less disturbing at present, owing to the fact that immigrants were mostly young people, the situation is, however, rapidly changing in face of diminished immigration.

The section on "Medicine and Religion" features an essay on "Sterilization and Eugenics in Jewish Law" by Rabbi I. Jakobovits, the Chief Rabbi of Ireland. The author discusses this controversial issue in the light of Jewish Law, and also presents the views of early Christianity, the medieval Church and the contemporary Roman Catholic Church on the subject.

This current issue is dedicated to the 750th anniversary of the death of Maimonides, the renowned Jewish medieval physician and philosopher. A series of articles in this issue deals with his life and outstanding contributions in the fields of medicine and philosophy. A biographical sketch on Maimonides is contributed by Dr. Moses Einhorn who cites some of Maimonides' memorable maxims of what makes a good doctor: "Besides the power to heal, a doctor must possess an independent mind; Medicine is necessary to man, not only when he is sick, but also when he is healthy; A doctor must be a whole man, observant, cautious, and attentive to each patient on the presumption that his case is individual and special."

Other articles on Maimonides deal with "The Influence of Religion and Philosophy upon Maimonides as Physician"; "Maimonides' Opposition to Occultism"; and "The Impact of Maimonides upon Medieval Writers in the Field of Medicine."

The editorial office of the Hebrew Medical Journal is at 983 Park Avenue, New York, N. Y.

The Fifty-Sixth Annual Meeting

OF THE

AMERICAN THERAPEUTIC SOCIETY

will be held at the

Shelburne Hotel, Atlantic City, New Jersey

on June 2, 3, 4 and 5, 1955